THE BRITISH
JOURNAL OF SURGERY

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JOURNAL OF SURGERY

VOLUME XXIII

July 1935 to April 1936. Numbers 89 to 92.

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THE

BRITISH JOURNAL OF SURGERY

IPSISSIMA VERBA

BY SIR D'ARCY POWER, K.B.E., LONDON

VI. TREVES' FIRST APPENDIX OPERATION

INFLAMMATION of the vermiform appendix and the possibility of surgical inter-
ference for its relief was beginning to attract attention in England in 1885 and in
Melbourne some three years earlier. The condition was still known as ' typhlitis ',
' perityphlitis ', and ' idiopathic peritonitis ', but no formal operation was under-
taken for its cure. The abscess was sometimes opened when the patient had
been fortunate enough to survive the suppuration and the measures taken to cure
it. The case reported by Mr. Frederick Treves appears to have been the first in
this country which was undertaken deliberately for the cure of a chronic and relapsing
inflammation, though he did not remove the appendix.

Mr. Charters J. Symonds[1] removed an appendix successfully at Guy's Hospital
on Aug. 24, 1883. The patient suffered from recurrent typhlitis associated with
a ' calculus ', but, in reporting the case afterwards, he said that he had seen 23 fatal
cases of typhlitis, but " thought that surgeons would long be deterred from opening
the abdomen and removing the appendix although such a proceeding might lead
to recovery in otherwise hopeless cases ".

Mr. J. H. Webb,[2] of Melbourne, gave bolder advice a year later and came
very near to anticipating Treves as a pioneer in the deliberate removal of the
appendix. He wrote that " three cases of perforation of the Vermiform
Appendix have occurred in my private practice during the last five years. All
have died and such lesions seem to be commoner than is generally supposed.
Drugs are useless but patients should not be left to die. The mind once made
up immediate action should be taken. I would certainly advise abdominal section
and if I ever have another case go through my hands I shall open the abdomen, say
Nay, who will. The operation will at least give a chance ." It does not appear that
Mr. Webb ever had the chance, for nothing more is heard of him.

The case reported by Mr. Treves[3] is in the following words. He was then
aged 34 and was full Surgeon at the London Hospital :—

" The following case afforded the only opportunity I have had of carrying
this proposed treatment into practice. The case was simple and the patient made
a sound recovery.

" A man, aged 34, a working engineer, was admitted into the London Hospital

under the care of Dr. Stephen Mackenzie, on December 31st, 1886, suffering from typhlitis. He had been a healthy, vigorous man of sober habits. He had had no illness except an attack of bronchitis fifteen years ago. He had been free from abdominal trouble previous to the present affection and his bowels had always been regular. Early in August, 1886, he was seized with pain in the right iliac fossa, followed by local swelling, vomiting, and constipation. This was his first attack of typhlitis. He was confined to bed and for a while improved under treatment, but after a week or so of freedom from pain, the symptoms reappeared with renewed vigour, the swelling and tenderness in the iliac fossa became once more pronouced, and the patient, to use his own expression ' was as bad as ever again '. Between the attacks he was not well enough to leave his bed, nor was he ever quite free from a sense of discomfort in the cæcal region. He was confined to bed for three months, i.e., from the commencement of August to the end of October. In November he was able to resume his work, and for a while did not complain of any trouble in his abdomen. He found, however, that his bowels did not act so freely after his illness as before. He remained well until December 27th—four days before his admission into the hospital—when he was once more seized with pain in the right iliac region attended by local swelling, sickness, and much prostration. He at once took to bed, but as his symptoms did not abate he came to the hospital.

" When admitted he presented the ordinary symptoms of typhlitis. He was well nourished and exhibited no organic disease other than that in the abdomen. A globular swelling occupied the right iliac fossa and was the seat of extreme tenderness. The abdomen was but slightly distended, the bowels were confined, but there was no vomiting. His temperature was 99·2° F. Opium was given and the constipation was relieved by enemata. His progress was very slow, the pain in the abdomen persisted, the swelling remained tender and diminished but sluggishly. It was not until February 8th, some six weeks after the commencement of the attack, that the abdominal symptoms had entirely disappeared. The patient was much weakened by his confinement in bed, but he did not complain of pain or tenderness in his abdomen, and no trace of any iliac swelling was left. Dr. Mackenzie now requested me to see the patient with reference to possible operative interference. Dr. Mackenzie was of opinion that the patient would be the subject of further attacks, and endorsed the suggestion that the abdomen should be opened and the cæcal region explored in the hope that the cause of the trouble might be removed.

" I performed laparotomy on February 16th [1887]. I opened the abdomen by a vertical incision immediately over the region of the cæcum. That part of the bowel was soon exposed. It was free from adhesions. There were evidences of old peritonitis about the appendix. To the base of that process the omentum had become adherent. The mesentery of the appendix was shrunken and had bent the tube upon itself at an acute angle. The part of the process on the proximal side of the bend was of normal aspect, that on the distal side was distended, was greatly thickened, and formed a rounded swelling the size of the end of the fore-finger. I had intended to remove the appendix, but it at once became straight on cutting away the omentum. I bared the convex side of the tube of peritoneum, thinking that fresh adhesions might occur upon that side and so hold the appendix in a straight position. The whole process only measured two inches and a half.

FREDERICK TREVES

I set free the omentum, sutured a small rent in the peritoneum that had been made during the examination, and closed the abdominal wound. It was evident that the shrinkage of the appendix mesentery had so bent that tube as to occlude it. Mucus had accumulated beyond the bend, and becoming retained had excited the peritonitis. The lumen had not become obliterated and the end of the diverticulum had apparently not been perforated.

"The patient recovered without a bad symptom. On March 18th, some little time after he was up and about, he had some slight pain in the seat of the old trouble. It was apparently due to constipation, as it disappeared at once on the administration of an aperient. The patient was kept in the hospital for another month, in order to be under observation. He remained perfectly well and has since that time had no further abdominal trouble.

" In the majority of cases it would probably be wiser to remove the appendix. If this is done as much care must be taken to close the divided end of the tube as would be taken to close a hole in the small intestine. A mere ligature would not be safe. Two sutures would suffice to bring the mucous membrane together, and the peritoneum should then be adjusted over this line of union by several points of Lembert's suture.

" It must be remembered that peritoneal adhesions or a peritoneum scarred by adhesions will not possess the same plastic power as the normal membrane.

" In the event of the process being so greatly thickened that suture of its serous coat is impossible I should be disposed to fix the stump to the nearest point on the surrounding parietal peritoneum."

The meeting at which the paper was read seems to have been well-attended, and in the subsequent discussion the President—Mr. Timothy Holmes, of St. George's—said that many years previously he had operated unsuccessfully on a somewhat similar case. Mr. Marsh and Mr. Walsham, of St. Bartholomew's, had been equally unsuccessful. Mr. Hulke, of the Middlesex Hospital, was in favour of operation but did not mention any case where he had done it. Dr. Hare preferred leeching ; Dr. Dickinson was wholly against operation, and Dr. Douglas Powell merely said that he thought the old term ' perityphlitis ' was better than ' inflammation of the vermiform appendix '.

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CARCINOMA OF THE GALL-BLADDER*

By C. F. W. ILLINGWORTH

SENIOR ASSISTANT SURGEON, EDINBURGH WESTERN HOSPITAL

IT is now well recognized that carcinoma of the gall-bladder is of quite frequent occurrence, but although numerous case reports and papers have appeared in the American and Continental literature, the subject has attracted little attention in this country. Its surgical importance, as a grave and generally fatal sequel to calculous cholecystitis, requires no emphasis.

During the last five years the writer has had the opportunity of making a close study of 30 cases, in the Edinburgh Royal Infirmary and the Western Hospital, and in addition has been given access to brief records of 20 other cases. Nearly all the cases have been under the care of Professor D. P. D. Wilkie, to whom the writer is deeply indebted for permission to put them on record.

HISTORICAL

The earliest reference to carcinoma of the gall-bladder appears to have been made by Maximilian Stoll, Professor of the Practice of Medicine in Vienna. In his *Ratio Medendi*, published in 1777, Stoll describes the post-mortem findings in three cases, all of which may reasonably be regarded as true examples of the disease under discussion, although later writers, following Courvoisier, have accepted only two.

Stoll's cases are described briefly, but succinctly. The first ("periit in ictero nigro ex scirrho sphincteris vesiculæ felleæ") is remarkable in having arisen in a left-sided gall-bladder with complete transposition of the viscera. In the second case, an old woman who suffered from chronic jaundice, the gall-bladder was "simul scirrhosa, callosa et cartilaginosa". Gall-stones were present in this case, the liver was "ulcerated", and the mesentery also was scirrhous. In Stoll's third case also the nature of the disease seems reasonably certain, for he records "periit in ictero chronico nigro: in exenteratione inveni hepar, collum vesiculæ felleæ, mesenterium et receptaculum chyli scirrhosum", and further evidence that the carcinoma originated in the gall-bladder is suggested by the final note, "bilis loco in vesiculæ fuit sanguis nigerrimus".

Eighteenth century writings contain only one other specific reference to carcinoma of the gall-bladder, by Hallé in 1786. Matthew Baillie's case, in which the coats of the gall-bladder, above a quarter of an inch thick, were "studded with tubercles of a considerable size and very firm", may also perhaps be included.

Thereafter the subject attracted little attention until the latter part of the nineteenth century, when a number of valuable papers appeared. Frerichs in 1861,

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in his treatise on diseases of the liver, remarked on the relation of gall-stones to carcinoma of the gall-bladder, whilst Musser (1889), Courvoisier (1890), and Ames (1894) gave excellent accounts of the disease. Indeed, it may be said that practically all our present knowledge of carcinoma of the gall-bladder, except upon the detailed histology, is derived from these writers, and more recent observations have served only to confirm and elaborate their findings.

FREQUENCY AND DISTRIBUTION

Frequency.—Numerous records from autopsy departments and surgical clinics indicate that carcinoma of the gall-bladder is far from rare. Lentze in 1926 was able to collect 890 case records, nearly all derived from German sources, whilst at least an equal number is to be found in the American literature.

It is difficult to give an exact estimate of. the true frequency of the disease, for many cases doubtless go unrecognized, and as a result the figures obtained from death certification are unreliable. Surgical statistics, being derived from selected groups of cases, probably give too high an impression of the frequency.

The most accurate estimate available is to be derived from the autopsy records of large general hospitals. In the post-mortem department of the Edinburgh Royal Infirmary during the last sixteen years there were 36 cases of carcinoma of the gall-bladder in a total of 8490 autopsies. During the same period the cases of malignant disease of all types and regions numbered 1275. Thus carcinoma of the gall-bladder accounted for 0·42 per cent of all autopsies and 2·8 per cent of all malignant disease.

Surgical experience shows that carcinoma is found in from 1 per cent to 2·5 per cent of all operations on the gall-bladder. Professor Wilkie informs me that in 1057 operations on the biliary tract he has encountered 34 cases of carcinoma of the gall-bladder, an incidence of 2·2 per cent. Deaver found 16 cases of carcinoma in 1000 operation cases ; Smithies 23 in a similar total ; whilst Judd and Gray, from the Mayo Clinic, have reported 212 cases from the large series of 22,365 operations on the biliary tract.

Sex Distribution.—All observers agree that a large proportion of cases occur in women. Fütterer in 1901 collected 264 cases from the literature, of which 204 affected women (77 per cent) ; and many later writers have reported a similar sex distribution. In the 50 cases reported in this paper there were 40 women, an incidence of 80 per cent.

Age Incidence.—Although there are records of carcinoma of the gall-bladder occurring at all ages from 22 to 95, the great majority fall into the age group 50 to 65 years, and the disease is distinctly rare before the age of 40 years.

In the present series the youngest patient was aged 39 years, the oldest 80 years. Thirty cases occurred between the ages of 50 and 65, and the average age was 60·6 years.

In the literature the youngest patient recorded is that of Proescher—an Italian male, aged 22, though in this case the diagnosis is not free from doubt. Shelley and Ross give references to three cases occurring at the age of 25 years, while there are a number of cases reported occurring between the ages of 28 and 30 years.

The literature contains numerous references to a case of Moxon's, which is stated to have occurred in a child aged 4 years, but reference to the original paper

shows that he has been misquoted.   Moxon did not mention the age of his patient, but his description of the patient's intemperate habits and his occupation as a brushmaker effectively disposes of the suggestion of childhood.

ETIOLOGY

Certain factors that require to be discussed in the etiology of carcinoma of other organs may be mentioned here only to be dismissed.   The presence of embryonic rests, for example, has rarely been suggested as a cause of carcinoma of the gall-bladder, except in connection with the uncommon squamous epithelioma, and even this remarkable tumour may be explained more convincingly on other grounds.   Nor is there any evidence to suggest that heredity plays an important part in the causation of the disease.

There remain two factors to be considered: (1) Simple papilloma of the gall-bladder; and (2) Cholecystitis and gall-stones.

Relation to Simple Papilloma.— Simple papillomata are of common occurrence in the gall-bladder.   They may be single or multiple, and occur as minute, green polypoid excrescences on the mucous surface.   Microscopically they have the characters of papillary, columnar-celled adenomata, and they are generally of quite benign appearance.

That these benign lesions bear any important relationship to carcinoma is highly improbable, as may be judged by the fact that Phillips has recently reported a series of 500 cases with no single instance of malignant degeneration.   There are, however, rare cases of multiple papillomata, which appear to form an intermediate link between the simple tumour and the papillary type of malignant growth.   The specimen shown in *Fig.* 1 is of this type. In it the gall-bladder mucosa is studded

FIG 1 —Multiple papillomata of the gall-bladder   The growths are of benign type, but in places show early invasion of the muscle coat   The condition may be regarded as precancerous

with minute papillomata throughout its whole extent.   Microscopic examination showed the growths to be of benign type, but with small areas of epithelial proliferation which extended in places through the muscle coat of the gall-bladder wall.   There is a close resemblance between this specimen and the papillary carcinoma shown in *Fig.* 2.

2. **Relation to Cholecystitis and Gall-stones.**—Almost all writers have drawn attention to the striking relation of gall-bladder carcinoma to gall-stones, and have differed only in their estimates of the frequency with which the two lesions coexist.   Thus Musser found that in a series of 100 cases of carcinoma of

the gall-bladder stones were present in 69 and definitely stated to be absent in only 3. Fütterer found stones to have been present in at least 70 per cent of the 209 cases he reported, whilst Siegert was of the opinion that stones coexist in 95 per cent of cases.

In the present series of 50 cases, stones were found in 31 and were undoubtedly absent in 7, whilst in the remaining 12 cases the presence of stones could not definitely be determined or had not been recorded.

These figures are highly significant, considering that in control cases of similar ages the incidence of gall-stones is less than 10 per cent, and there can be no doubt that there is a definite relationship between gall-stones and carcinoma of the gall-bladder. That the stones have been present before the carcinoma has originated,
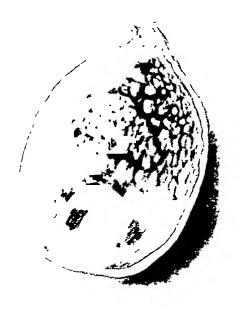
FIG 2.—An early carcinoma of the gall-bladder of the papillary type. At operation the large gall-stone was found impacted at the neck of the gall-bladder, in contact with the growth.
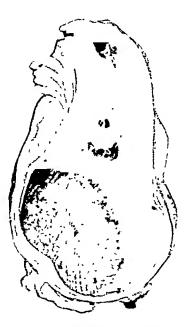
FIG. 3.—Scirrhous carcinoma of the gall-bladder. At operation the solitary stone was found impacted near the neck of the gall-bladder. The viscus was acutely inflamed and contained mucopus.

and are not secondary formations due to the biliary obstruction caused by the growth, is proved by the fact that in most cases the stones are well consolidated, with a structure indicative of long formation. Moreover, in some cases the growth originates at the neck of the gall-bladder where the mucosa is ulcerated by the pressure of an impacted stone (*Figs.* 2, 3).

Several writers have suggested that stones predispose to carcinoma of the gall-bladder in virtue of some special constituent, for it is known that gall-stones contain traces of many minerals, such as copper, iron, and manganese, in addition to cholesterol, calcium, and bile pigments. Lazarus-Barlow has shown that a small proportion of gall-stones contain radio-active salts, and has suggested that the origin of the carcinoma is due to their long-continued irradiation. At present,

however, this view lacks confirmation. Perhaps future researches will demonstrate the presence of a specific agent similar to dibenzanthracene, or the active hydrocarbons occurring in carcinogenic tars.

It is interesting to note that there are a number of cases on record in which a carcinoma has originated several months or even years after the stones have been removed by cholecystotomy. Many years ago Knaggs, Mayo Robson, and Lett recorded single instances of this sequence of events, and several other cases have been reported recently. In 84 gall-bladder carcinomata reported by Magoun and Renshaw there were 5 in which previous cholecystostomy had been performed. In its tendency to occur after the predisposing agent has been removed carcinoma of the gall-bladder is comparable to tar cancer, to the skin epithelioma of mule-spinners and shale-workers, and to other forms of carcinoma arising as the result of chronic irritation.

Whilst attention has been directed mainly to the relation of carcinoma to gall-stones, an even more important predisposing factor is the presence of cholecystitis. There are undoubted cases of carcinoma of the gall-bladder without stones, but a pre-existing cholecystitis appears to be the invariable rule. It is doubtful if carcinoma ever starts in a healthy gall-bladder, and it is thus one of the most perfect examples of a malignant growth arising as a result of chronic irritation.

The risk of carcinoma developing in patients with calculous cholecystitis is by no means inconsiderable, as has been shown by numerous statistics based on experience both in the autopsy department and in surgical clinics. Thus Riedel, in his paper on gall-stones published in 1901, stated that in the course of five or six hundred gall-stone cases seen by him there were no fewer than 43 cases of carcinoma (7 to 8 per cent), whilst Fawcett and Rippmann found that malignant change had supervened in no fewer than 48 (8·1 per cent) of 592 gall-stone cases seen in the autopsy department of Guy's Hospital.

Whilst it is probable that these figures, derived as they are from selected groups of cases—namely, those in which the symptoms were sufficiently severe to necessitate admission to hospital—tend to give a somewhat exaggerated idea of the frequency of malignant degeneration, they nevertheless indicate that the risk is by no means inconsiderable.

From the clinical standpoint it is important that this risk should be fully appreciated. When a carcinoma of the gall-bladder is fully established, there is little prospect of being able to extirpate it completely. Our aim must therefore be to prevent its occurrence, and this can only be achieved by early operation. And since a carcinoma may arise even after removal of the stones, the only certain method of prevention is by the performance of cholecystectomy.

EXPERIMENTAL PRODUCTION OF CARCINOMA OF THE GALL-BLADDER

A number of attempts have been made to produce carcinoma of the gall-bladder in animals, but with little success. This is not surprising, considering that it is notoriously difficult to initiate a carcinoma in any columnar-celled membrane, and especially in view of the fact that spontaneous gall-bladder carcinoma in animals in unknown.

Kazama in 1912 claimed to have produced carcinoma in guinea-pigs by inserting such foreign bodies as pebbles, suture material, and lanoline into the gall-bladder. In a series of 98 guinea-pigs he claimed that cancer was produced in 26.

Leitch repeated these and similar experiments, inserting gall-stones, pebbles, and pilules of pitch into the gall-bladder. When the animals were killed from five to twelve months later, the gall-bladder wall was found to be thickened and indurated, and microscopic examination showed areas that appeared to be carcinomatous. Subsequent work, however, appears to indicate that these lesions were not malignant, and that the epithelial proliferation was simple in type, a response to the chronic irritation of the foreign bodies.

Since then, Clemente, Delbet and Godard, and others have performed similar experiments, using tar, gall-stones from cancerous patients, and other foreign bodies.

Burrows has recently summarized all the literature on this subject and has repeated the experimental work, inserting gall-stones derived from non-cancerous patients into the gall-bladders of guinea-pigs. He points out that there are certain fallacies attending the microscopic diagnosis of carcinoma after such experiments, for the remarkably active proliferation of glandular structures and young bile-ducts as a result of the irritation may easily be mistaken for malignant growth. Burrows' work indicates the need for caution in assessing the previous experimental findings, and the claims of certain workers to have produced carcinoma of the gall-bladder experimentally cannot be regarded as substantiated.

THE PATHOLOGY OF CARCINOMA OF THE GALL-BLADDER

We may recognize four principal types of carcinoma of the gall-bladder, which may be distinguished from each other fairly readily by either naked-eye or microscopic examination: (1) Scirrhous carcinoma; (2) Papillary carcinoma;

FIG. 4.—Scirrhous carcinoma of the gall-bladder, giving rise to an hour-glass deformity. The greater omentum is adherent to the distal sac, which is obstructed and inflamed.

(3) Mucoid or colloid carcinoma; (4) Squamous-cell carcinoma or epithelioma.

1. **Scirrhous Carcinoma.**—This is quite the commonest type of growth seen in the gall-bladder. It is a hard infiltrative tumour, which starts as a localized thickening or induration of the gall-bladder wall, and gradually spreads to encircle or ultimately to envelop that viscus. At an early stage it may be mistaken for

an area of chronic cholecystitis, and if, as often happens, it arises in a gall-bladder already thickened and indurated as a result of chronic cholecystitis, it may easily be overlooked unless routine microscopic examinations are carried out.   Later, the presence of the growth will be recognized by the degree of induration, for it may be as hard as cartilage.

The growth may originate at the neck of the gall-bladder, at its mid-point, or at the fundus.   In the series reported here the growth had started at or close to the neck of the gall-bladder in 6 cases, near the mid-point in 2 cases, and at
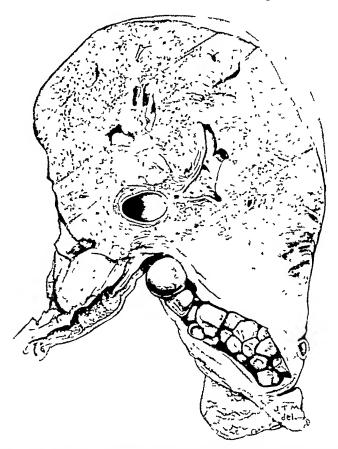
Fig 5 —Scirrhous carcinoma, completely enveloping the gall-bladder and invading the liver   The adherent omentum is infiltrated by the growth, and a secondary nodule is seen in the cystic lymph gland

the fundus in 3 cases.   In the remainder the growth was so extensive that its site of origin could not be demonstrated.

If the tumour arises at the neck of the gall-bladder, it may constrict the cystic duct and lead to a mucocele or an empyema of the gall-bladder, as happened in one of the cases recorded here (*see Fig.* 3).   A tumour arising in the body of the gall-bladder may give rise to an hour-glass deformity, as in the case illustrated in *Fig.* 4.

Eventually, a scirrhous growth may infiltrate the whole gall-bladder, enveloping
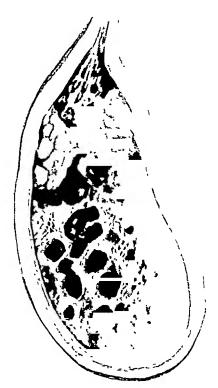
it completely in a dense mass of malignant tissue (*Fig. 5*). Indeed, the gall-bladder may be so buried in the growth as to be difficult to find, even at autopsy, and the only clue to its situation may be a collection of gall-stones, packed tightly in the centre of the tumour. Sometimes, as the tumour contracts upon the lumen of the gall-bladder, the stones are extruded into the common bile-duct.

FIG. 6.—Scirrhous carcinoma of the gall-bladder. The tumour is an adenocarcinoma, and contains irregular acini lined by columnar and cubical cells.

The microscopic structure of a scirrhous tumour of the gall-bladder is that of an adenocarcinoma (*Fig. 6*). There are acini or tubules, lined by columnar or cubical cells, set in a stroma of dense fibrous tissue. The epithelial cells are often of low columnar type, and evidence of their secretory activity may be furnished by the presence of mucin within the acini.

In most cases the cells are obviously malignant, but in others the appearance is not greatly different from that of the normal cells of the mucosa, and indeed it may occasionally be difficult to distinguish the acini of a carcinoma from the glandular proliferations sometimes seen in chronic cholecystitis—the so-called cholecystitis glandularis proliferans.

FIG. 7.—Papillary carcinoma of the gall-bladder. The tumour was cut across when the gall-bladder was opened, and its two halves are displayed. The tumour is pedunculated and nodular, and to the naked eye appears benign, but its malignant character is evident on microscopic examination.

When it is remembered that acini of a somewhat atypical appearance may penetrate the muscle coat in chronic cholecystitis (the Rokitansky-Aschoff sinuses) and that similar deeply placed tubules are sometimes found in the healthy gall-bladder (Luschka crypts), the difficulty in diagnosing an early carcinoma will be apparent.

2. **Papillary Carcinoma.**—This is less common than the scirrhous growth. It is a softer and often a more bulky tumour, and it

does not infiltrate so extensively, but rather tends to grow into the cavity of the gall-bladder.

At an early stage it may consist of multiple small villous outgrowths of the mucous membrane, rather resembling a malignant papilloma of the urinary bladder. The specimen shown in *Fig. 2* is of this type. Rarely there is a solitary, pedunculated tumour, which may appear to be benign until examined microscopically (*Fig. 7*). Later the tumour may attain quite considerable size, partly filling the gall-bladder. It is prone to hæmorrhage and necrosis, and may be so soft as to be mistaken for inspissated pus.

The microscopic appearance is that of a columnar-cell adenocarcinoma with a scanty connective-tissue stroma. Often a definite papillary arrangement is recognizable.

3. **Mucoid or Colloid Carcinoma.**—This type of growth is not uncommon in the gall-bladder. The tumour is generally somewhat bulky and soft, and its character may be recognized by the jelly-like appearance of the growth. Sometimes the whole tumour is of mucoid type, more often only a part is affected, and in some cases the condition may only be discovered on microscopic examination. In the present series some degree of mucoid change was observed microscopically in several cases. In only one, however, was it so extensive as to be recognizable on naked-eye examination.

FIG. 8.—Mucoid carcinoma of the gall-bladder. There are a few ill-formed acini lined by columnar cells, scattered like small islands in a sea of mucin.

Microscopically there is a stroma consisting of trabeculæ of fibrous tissue, interspersed with large spaces containing a structureless, blue-staining material—pseudomucin. The tumour cells are few in number and lie singly or in small groups or ill-formed acini, often scattered like small islands in a sea of mucin (*Fig. 8*). The cells contain small droplets of mucin in their cytoplasm, and some of them are swollen to 'signet-ring' shape by a large globule of this substance, which distends the cell membrane and forces the nucleus to one edge. A cell thus distended may burst, discharging its mucinous content into the connective-tissue spaces.

4. **Squamous-cell Carcinoma or Epithelioma.**—This remarkable tumour is the least common form of gall-bladder carcinoma. In the present series of 30 cases there was only one complete example—that is, one in which all parts of the tumour were of squamous character. In two other cases a partial squamous-cell change had supervened, giving rise to the extraordinary appearance of areas of squamous epithelioma adjoining and merging into areas of columnar-cell adeno-carcinoma.

To the naked eye, tumours of this class generally appear of scirrhous infiltrating character, and the peculiar nature of the growth is only recognizable on histological examination.

Microscopically, parts of the tumour, or in some cases the entire growth, present the characters of an epithelioma, such as are seen in tumours of the skin, the tongue, or the œsophagus. The cells are of squamous type, and it is some-
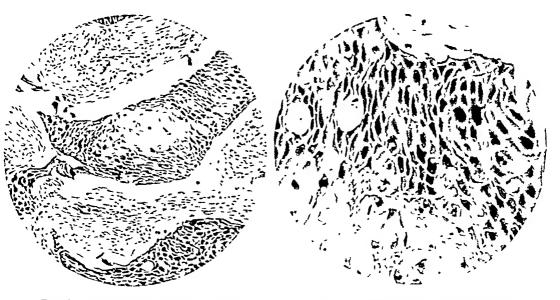
FIG 9 — Squamous-cell carcinoma of the gall-bladder showing typical cell-nest formations (120)

FIG 10 —Squamous-cell carcinoma of the gall-bladder showing the presence of prickle cells with intercellular bridges (∧ 400)

times possible to identify typical prickle cells with intercellular bridges. Cell nests or epithelial pearls occur, though rarely, for keratinization is not a marked feature of these tumours (*Figs.* 9, 10).

The special interest of squamous epithelioma of the gall-bladder lies in the fact that it occurs in a columnar-cell epithelium derived from entoderm. The gall-bladder is derived by a process of budding from the biliary diverticulum, which arises from the intestine at the junction of foregut and midgut, and at no period of embryonic life is it related to a squamous-cell membrane.

There is therefore no reason to attribute an epithelioma of the gall-bladder to the persistence of epithelial rests of squamous type, nor is there, at first thought, any explanation based on embryological grounds.

It seems probable that epithelioma in the gall-bladder should be regarded as

the result of a process of metaplasia, whereby the cells of the mucous membrane, originally cylindrical, have reverted to their primitive form and subsequently assumed squamous characters.

Nicholson has pointed out that such a change has its analogy in the normal development of the œsophagus. The œsophagus is derived from the primitive foregut, and, as Schaffer and Keibel have shown, its lining membrane, like that of the remainder of the foregut, originally consists of a layer of ciliated cylindrical cells. Whereas in the remainder of the foregut the cells retain their cylindrical form, in the œsophagus at an early stage in embryonic life they are entirely converted to squamous type. This potentiality for squamous metaplasia, normally seen only in the œsophagus, is found occasionally in the cells of the cardiac end of the stomach, and it is quite conceivable that it may be retained in exceptional cases by the cells of the lower part of the foregut close to the point from which the gall-bladder is derived.

The customary explanation of epithelioma of the gall-bladder is that it arises in a part of the gall-bladder wall affected by leukoplakia. As a result of chronic irritation by gall-stones or cholecystitis, the epithelial cells of the mucous membrane assume squamous form, whilst further irritation leads to their developing malignant characters.

THE SPREAD OF CARCINOMA OF THE GALL-BLADDER

In the great majority of cases carcinoma of the gall-bladder spreads by direct invasion of neighbouring viscera and regional lymph-vessels. The growth disseminates to distant organs rarely, even in its terminal phase; quite early in its course, however, it invades locally and oversteps the limits of successful removal.

The *liver* is generally the first organ to be invaded. It was involved in all the 14 cases of the present series examined post-mortem and in 12 of the 16 cases seen at operation. In the remaining four cases there were no evident metastases, and in each the gall-bladder was removed.

Generally the tumour spreads by direct continuity from the gall-bladder to the adjoining part of the right lobe of the liver and forms there a solitary, hard, and often bulky mass. The remainder of the liver is usually unaffected, but in a small proportion of cases there are multiple secondary nodules scattered through both lobes. Less often the liver is invaded by a branching growth spreading along the periportal lymph-vessels from the lymph nodes in the porta hepatis.

The *regional lymph nodes* are involved almost as often as the liver, and their involvement may preclude successful operation in cases where the extirpation of a localized mass invading the liver might otherwise be attempted.

The cystic lymph node, which lies on the under aspect of the cystic duct, is involved first, and from there the disease spreads to the nodes in the right free border of the lesser omentum, in the porta hepatis, and in the retroperitoneal tissues. In many cases the jaundice observed in carcinoma of the gall-bladder is due to the pressure of secondary nodes upon the common bile-duct. In autopsy cases lymph-borne metastases are occasionally found in the mediastinal, tracheo-bronchial, and even the cervical lymph nodes.

The *peritoneum* is involved quite often in the later stages of the disease. It is said that this is most likely to occur when the tumour is of mucoid type. *Multiple*

secondary nodules then develop on the peritoneal surfaces and malignant ascites rapidly supervenes. There is one case on record (Wakasugi) in which a large metastasis on the pelvic floor simulated a carcinoma of the rectum.

The *omentum* is involved in a number of cases, especially if it be adherent to the gall-bladder as a result of cholecystitis.

The *duodenum*, the *colon*, and even the *jejunum* may be involved by direct invasion, and fistulæ between the gall-bladder and these viscera are not uncommon. In some cases when invasion of this type occurs early the clinical features may suggest the presence of a primary tumour at the pylorus or in the right colic flexure.

Distant metastases are uncommon, even in autopsy cases. There are a few instances on record, however, in which distant metastases have occurred so early in the course of the disease as to provide the first clinical evidence of it.

The *lungs* are involved in about 10 per cent of cases. The pulmonary metastases are generally multiple, of small size, and mainly situated close under the pleura. The growths are most numerous in the lower lobe of the right lung, and it seems probable that they reach that situation by spreading along the retro-diaphragmatic lymphatics.

In one case, reported recently by Foggie and Tudhope, there was a solitary metastasis in the upper lobe of the left lung. In this case the primary tumour was inconspicuous, and was discovered only at autopsy. In a case reported by Osler in 1906 a nodule in the right breast, which simulated a primary mammary carcinoma, was the first demonstrable evidence of the disease.

The *bones* have been the site of metastatic growth in a few reported instances. Beadles in 1897 reported a case in which the first evidence of disease was provided by a tumour arising in the second rib. The tumour increased in size during four months, infiltrating the pectoral muscles but not invading the pleura, and eventually it attained the size of a coco-nut. Only at post-mortem examination was the primary growth found.

CLINICAL FEATURES

Since carcinoma of the gall-bladder is almost invariably imposed upon a former cholecystitis, generally with gall-stones, we should expect that in the majority of cases an old history of biliary disease would be forthcoming. Such a history was obtained in 16 of the 30 fully recorded cases in the present series, dating back five, ten, or even thirty years. In the majority the symptoms were of the type generally associated with chronic cholecystitis—flatulent indigestion, pain below the right costal margin, and occasional attacks of biliary colic. In several cases there had been one or more attacks of jaundice. In one case cholecystostomy had been performed seven years before.

It is surprising that in as many as 14 cases no history of previous disease was obtainable, and this is in accord with the observations of other writers. To some extent, doubtless, this is due to faulty anamnesis. Leading questions are required to elicit a history of relatively mild digestive upset, in a patient in the late stages of malignant disease. In this connection it is noteworthy that, in the present series, a former history of biliary disease was obtainable much more frequently in the surgical cases than in those seen at autopsy. Even allowing for this, however,

there remains a certain proportion of cases in which a previous history is entirely lacking.

Typical Cases.—In typical cases a carcinoma of the gall-bladder gives rise to pain, associated with anorexia, nausea, and vomiting, and followed by jaundice, whilst examination may reveal a palpable swelling under the right costal margin.

The pain is at first not severe, and may be regarded merely as indigestion. It is generally of dull, aching, or gnawing nature, continuous, and unrelated to food. It is situated over the gall-bladder region, and in most cases radiates to the right scapula or the loin. Occasionally, referred pain is felt in the left hypochondrium or in the lower part of the abdomen, whilst in rare cases there is a definite history of pain at the tip of the right shoulder. The pain is rarely colicky, but in the late stages is often severe. In a few cases, however, pain is not a prominent feature. In two cases in the present series the disease was painless throughout.

Nausea was a recorded symptom in every case. Vomiting occurred in most cases, but was rarely severe or persistent. Anorexia, flatulent distension, and occasionally diarrhœa were other features.

Jaundice was noted at some stage of the disease in 16 of the 30 cases. Typically, it is of late occurrence, due to pressure by secondary growths upon the common duct. It is important to observe that jaundice is not necessarily a bar to successful operation. In two cases in the present series the jaundice was due to the presence of stones in the duct—in one of these the growth was limited to the gall-bladder and was removed—whilst in a third the jaundice was due to cholangitis, with multiple liver abscesses.

A palpable swelling in the subcostal region is a frequent finding in the late stages of the disease. It was noted in 18 of the 30 cases in the present series. Generally the swelling is of stony hardness and is due to the growth itself, enveloping the gall-bladder and infiltrating the liver. Less often the swelling is due to mucocele or empyema of the gall-bladder behind a tumour located near the cystic duct.

It is important to recognize that loss of weight is not a common finding in carcinoma of the gall-bladder. The tumour may attain large size and spread extensively with little or no disturbance of the general nutrition. Pronounced loss of weight was noted in only 8 of the 30 cases, whilst in 11 cases it was definitely stated that no loss of weight had occurred, and in many of the remainder the patient was noted as well-nourished, stout, or even obese.

Atypical Cases.—The present series includes a number of cases in which the symptoms differ from those described above, and many others are recorded in the literature. For convenience, they may be divided into three groups.

1. *Symptoms Mainly Due to Obstruction of the Common Duct.*—Five of the present series fall into this group. The primary growth is symptomless or almost so, and the clinical features are mainly due to pressure by the growth or by metastatic nodules upon the common duct. In these cases jaundice is an early feature. It is painless in onset, progressive in course, and ultimately intense. Since the gall-bladder may be palpably enlarged, the condition is apt to be mistaken for carcinoma of the pancreas or of the common duct. The progress in these cases is rapid, and death may occur within a few weeks of the onset of the jaundice.

2. *Symptoms Mainly Due to Obstruction of the Cystic Duct.*—Three of the thirty

cases fall into this group. They are exemplified by the following case, in which the clinical features were those of empyema of the gall-bladder. A woman aged 62 years, who gave an old history of biliary trouble, was admitted to hospital with acute pain in the right subcostal region, radiating to the back. There was slight pyrexia, no jaundice. Abdominal examination revealed an enlarged, very tender gall-bladder, protected by muscular boarding. At operation the gall-bladder was distended, inflamed, and surrounded by soft omental adhesions. It was opened and found to contain mucopus and a single stone, impacted at the neck. Further examination revealed the presence of the growth, and accordingly the gall-bladder was removed. (*See Fig.* 3.)

3. *Symptoms Mainly Due to Secondary Growths.*—In five cases in the present series the first symptoms were due to secondary growths. In two of these widespread peritoneal metastases gave rise to abdominal pain mainly located in the umbilical region and the lower part of the abdomen, with vomiting, diarrhœa, ascites, and rapid progress to a fatal issue. In one case a secondary growth invading the duodenum gave rise to pyloric obstruction with hæmatemesis and melæna. In two cases the symptoms appeared to be due to widespread involvement of the liver, and were characterized by repeated retching and vomiting, with pain over the enlarged liver, slight jaundice, and marked toxæmia.

TREATMENT AND PROGNOSIS

At the present time the majority of cases are seen too late for radical removal of the tumour, and although it is sometimes possible to relieve the symptoms to some extent either by draining the gall-bladder if distended, or by establishing biliary drainage if the common duct is compressed, such procedures can clearly be of limited value.

The probable duration of life in such cases is generally short. The immediate mortality alone is high, for in many cases jaundice is present at the time of operation and cannot be relieved. Those who survive the immediate post-operative period generally succumb within a few months.

In a small proportion of cases, however, where the growth is found at an early stage, the results of surgical treatment are more satisfactory. If the growth is limited to the gall-bladder wall, complete extirpation may be achieved, whilst even when there is local invasion of the liver, excision of the affected portion of that viscus may be carried out. It must be admitted, however, that this is only rarely possible.

The difficulty of treating an established carcinoma of the gall-bladder emphasizes the importance of preventing its occurrence by radical treatment of its main etiological factor, calculous cholecystitis. When it is borne in mind that malignant disease is the eventual outcome in a by no means inconsiderable proportion of all gall-stone cases, it will be seen that the benefits of timely operation far outweigh the risks. The observation that carcinoma may develop years after the stones have been removed by cholecystostomy indicates that removal of the gall-bladder is the operation of choice.

This paper is the outcome of work carried out in the Department of Surgery of the University of Edinburgh, and is based upon cases seen in the Edinburgh

Royal Infirmary and Western Hospital. The writer wishes to acknowledge his debt of gratitude to Professor D. P. D. Wilkie for permission to make use of his cases, and for his constant encouragement in the production of the paper; to the staff of the Department of Surgery for their technical co-operation; and, lastly, to Colonel W. F. Harvey, of the Laboratory of the Royal College of Physicians of Edinburgh, for the use of the excellent photomicrographs illustrated in *Figs.* 9 and 10.

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THE OPERATIVE TREATMENT OF FIBROUS STRICTURE OF THE RECTUM:

WITH THE DESCRIPTION OF A NEW TECHNIQUE

By J. P. LOCKHART-MUMMERY

EMERITUS SURGEON, ST. MARK'S HOSPITAL, LONDON

AND O. V. LLOYD-DAVIES

ASSISTANT SURGEON, ST. MARK'S HOSPITAL

SIMPLE, or fibrous, strictures of the rectum are met with in very many different forms, but all the cases can be roughly divided into two main types, tunnel strictures and ring strictures.

Fibrous strictures of the rectum result from the contraction of scar tissue caused by injury or severe inflammation in the rectal wall or the tissues immediately around it. The contracting scar tissue may be localized to one particular part of the rectum, and result from accidental or operative trauma, or from a localized ulcer or abscess, or it may be due to a general inflammation of the rectum and surrounding tissues. Any of the ordinary forms of septic infection may be responsible for the condition, and there are also certain more or less specific forms of infection such as gonorrhœal infection of the rectum, tertiary syphilis, and fourth disease or lymphangitis inguinale.

We do not propose to discuss here the etiology of rectal stricture, or the difficult question of the relation of syphilis to the condition, beyond saying that it is now generally agreed that syphilis is a very rare cause and that antisyphilitic treatment seldom results in any improvement, though in doubtful cases it should be given a trial before proceeding to operative interference. Whatever the original cause may have been, the condition which the surgeon is called upon to treat is a late result of old-standing inflammation. As a rule it is only after a long period of chronic inflammation, often lasting several years, that the stricture becomes sufficiently severe to call for operative interference.

The diagnosis is not always easy, and it is important to ascertain the type of stricture and its extent. It is generally advisable to administer an anæsthetic, preferably a low spinal injection, and then partly to dilate the stricture so that its upper limits can be explored and the condition of the bowel immediately above ascertained. A very fine bore sigmoidoscope can usually be passed through the stricture and the condition of the bowel above investigated. Needless to say, great care must be exercised not to split the rectal wall and set up a perirectal inflammation. There is almost always in cases of old stricture a severe degree of local sepsis present, and before proceeding to any operative attack upon the stricture this must be cleared up as far as possible. The stricture should be dilated as much as is safe and treated by frequent douching with mild antiseptics. In very severe cases a preliminary temporary colostomy will be necessary.

ANNULAR DIAPHRAGMATIC STRICTURE

The choice of treatment will depend very largely upon the situation of the stricture. If it is situated at the anus or in the lower part of the rectum, below the peritoneal reflection, it can be dealt with comparatively easily. The best method is by internal proctotomy and dilatation. The stricture is nicked with a blunt-pointed bistoury in several places posteriorly and laterally, but not anteriorly, and then rapidly dilated up to an inch in diameter with metal dilators. The rectum is then thoroughly washed out with antiseptic, and partly filled with sterilized vaseline. A large rectal tube, preferably of vulcanite, of the same size as the largest rectal dilator is inserted into the rectum and retained for two days. After this the stricture is kept dilated by passing a full-sized dilator, at first daily and then at longer and longer intervals. This should continue for about three months until all sign of stricture has disappeared.

The results of internal proctotomy are excellent and permanent, if the patient is willing to put up with the inconvenience of dilating the site of the stricture for long enough to counteract the tendency to recurrent contraction in the scar tissue. This is the method that has been used for years at St. Mark's Hospital for this type of stricture, and the results have been uniformly satisfactory.

This method is not applicable where the stricture is very high up and near, or above, the peritoneal reflection, as there would be serious risk of tearing the bowel into the peritoneal cavity. In the case of a thin diaphragm stricture situated high up, internal proctotomy can sometimes be performed successfully if great care is taken and the cutting of the diaphragm is done visually through an operating sigmoidoscope. The dangers of dilating high-lying strictures of the rectum are so serious that such treatment is best not attempted. High strictures are best treated by resection or colostomy, or by the plastic method described here.

TUNNEL STRICTURES

This type of stricture (*Fig.* 11) cannot be dealt with by internal proctotomy, and dilatation is very unsatisfactory, as it involves the constant use of dilators, usually with little benefit and much pain. The alternatives are permanent colostomy, resection of the strictured portion of the rectum, and, in suitable cases, the method described here. Colostomy is sometimes the only possibility, and, where a serious degree of stricture with bad local sepsis exists, may have to be permanent. In most cases a temporary colostomy is the first step in the procedure, and if there is a possibility of restoring the rectum a transverse colostomy should be performed, both because it is more easily and safely closed again, and because it leaves the pelvic colon free to be brought down if a resection of the stricture is to be performed later.

The best known method of resecting a rectal stricture is that of Hartmann. The rectum is exposed through a posterior incision after removing the coccyx. The bowel is then divided above the stricture and dissected out to the skin margin at the anus without damaging the sphincter, and the proximal end of the colon is brought down and fixed to the skin at the anal margin. Hartmann records 34 cases treated by resection, with 2 deaths.

The chief difficulty of the resection operation is to get the parts sufficiently

free from gross sepsis to render any operation reasonably safe. There is often a free discharge of pus from the rectum, and numerous fistulæ discharging on the skin surface. A preliminary colostomy, followed for some weeks or months by frequent irrigation of the strictured bowel from the lower colostomy opening, will often clear up the septic condition sufficiently to make operation on the stricture
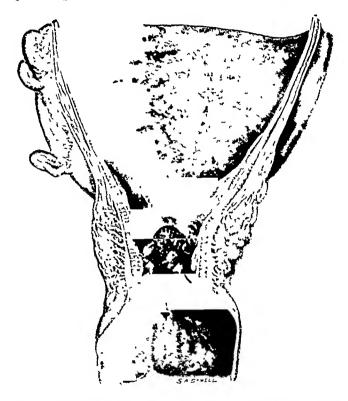
FIG 11 —Drawing of a specimen of fibrous stricture of the rectum in the Royal College of Surgeons Museum, showing dense fibrosis of the perirectal tissues

possible (*Fig.* 12). Even then the operation is by no means easy owing to the dense fibrous tissue present in the cellular tissues around the bowel that has to be removed. The combination of sepsis and fibrous adhesions round the bowel render the operation of resection more difficult in cases of fibrous strictures than in malignant disease.

NEW TECHNIQUE

In the following case a procedure was adopted which we believe to be original and seems to offer an alternative to Hartmann's method of resecting the stricture. It has the merit of being both simpler and safer, and, at any rate in this case, gave a better result than could have been obtained by resection. It is obvious that it is not applicable in all cases of fibrous stricture of the rectum, as it is essential that free access should be obtainable to the whole of the strictured area. On the other

hand, since the operation does not involve opening the peritoneum, it is very much safer than a resection operation.

HISTORY.—The patient was a married woman, aged 32. Thirteen years ago, after a bad confinement, she had a profuse discharge of blood and pus from the rectum, associated with abdominal pain and fever. The discharge failed to respond to any treatment, and some years later she was found to be suffering from a severe rectal stricture. Various attempts were made to dilate the stricture without success, and six years ago a colostomy was performed in the pelvic colon. After this the discharge from the rectum gradually ceased, and her general health much improved, but she became very desirous of getting rid of the colostomy opening. She was admitted to St. Mark's Hospital in the hope that something could be done to the stricture to enable the colostomy to be closed.

FIG. 12 —Photograph of a specimen of fibrous stricture of the rectum   The patient was a woman aged 40   The strictured portion of the rectum was resected and the rectum restored after a temporary colostomy. She has remained well since

ON EXAMINATION.—A well-marked tubular stricture was found about 3 in. in length and situated in the middle and upper part of the rectum. The mucous membrane lining the stricture was ulcerated, but the mucous membrane above, as seen by passing a small sigmoidoscope through the lower colostomy opening, was normal in appearance, as was that of the lower rectum.

An attempt was then made to heal the ulceration by introducing 4 oz. of a suspension of bismuth subgallate (5 per cent) in cotton-seed oil into the lower colostomy opening each night, and washing through every day with a solution made by adding 1 drachm containing equal parts of sodium chloridi, sodium bicarbonatis, and pulv. ac. borici, to one pint of water. At the end of three weeks examination showed that the ulceration had healed, and it was decided to operate on the stricture

by dividing it longitudinally from behind and suturing it in a transverse manner similar to the method used in performing a pyloroplasty for stricture of the pylorus.

OPERATION (*Fig.* 13).—The patient was given a low spinal anæsthetic and then placed in the Sims position. The rectum was thoroughly washed out with a weak antiseptic solution and an incision was made in the mid-line posteriorly, extending from a point over the lower part of the sacrum to a point just behind the anal orifice. The coccyx was removed and the post-rectal fascia divided. The rectum was then freely mobilized by stripping it from the pelvic wall on each side. In this way it was possible to draw down into the wound that part of the rectum containing the stricture. A considerable amount of dense fibrous tissue had to be divided before the actual rectal wall could be exposed, and the stricture was then divided longitudinally into the rectum, the incision extending into healthy bowel both above and below the narrowed portion. Tissue forceps were then placed on the edge
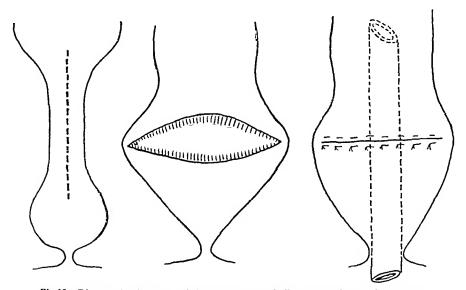
Fig. 13.—Diagram showing steps of the operation for dealing with stricture of the rectum.

of the rectal wound on each side in the middle of the longitudinal incision and the rectum was drawn open. A large rubber tube was next passed into the rectum through the anus, the upper end passing well above the strictured area. The incision in the rectum was then closed transversely by interrupted catgut sutures with the knots on the mucous side, and covered by a second line of Lembert sutures. The fascia was then stitched over the line of suture and the skin closed, a small drain being placed in the upper part of the wound. The drainage tube in the wound was removed in twenty-four hours and the rectal tube in four days. Satisfactory healing took place except for a small sinus, which healed in a few weeks. On examination of the rectum no sign of stricture was present and it was possible to pass a No. 26 Hegar dilator very comfortably and with no pain.

SUBSEQUENT HISTORY.—The patient went home, and returned four months later for closure of the colostomy. The rectum was still well dilated, there was

no sign of stricture, and the colostomy was closed intraperitoneally. The abdominal wound healed very satisfactorily, and the patient returned home three weeks later.

It is now a year since the closure of the colostomy, and the patient's bowels are open normally and regularly every day, and there is no sign of the original stricture.

We have not been able to find any description of a similar operation for fibrous stricture of the rectum, and believe that this is the first time this operation has been performed. The result is so eminently satisfactory that we consider it worth while publishing. It is obviously a much less severe operation than a resection of the rectum, and is not particularly difficult. It has the great merit of leaving the patient with a normally functioning rectum and perfect control, since there is no damage to the muscles of the anal opening.

In order to be successful it would seem essential that all local sepsis should be cleared up before performing the operation, and a temporary colostomy would seem advisable. In performing the operation, the rectum must be thoroughly freed so that no tension will come on the sewn-up wound in the rectal wall.

NOTOCHORDAL TUMOUR OF THE CAUDA EQUINA IN A CHILD OF 8 YEARS

By V. H. ELLIS

ORTHOPÆDIC SURGEON TO ST. MARY'S HOSPITAL, LONDON

TUMOURS of the notochordal remnant have attracted increasing attention during the last few years, and the diagnosis and treatment of tumours of the spinal cord have also made great advances. The following case, therefore, may have points of interest under both these heads.

The derivation of tumours from the notochord was established by Ribbert[1] in 1894, but the groundwork for his researches was laid by Muller[2] in 1858, and there are records of earlier observations. Since that time many cases have been described and several reviews of the subject published, such as that by Stewart[3] (1926).

The site of the great majority of tumours described has been occipital or sacro-coccygeal, the former arising in connection with the anterior, and the latter with the posterior, extremity of the notochord. Aberrant notochordal vestiges have occasionally been found, and Coenen[4] published a review of such cases in 1925. Unlike chordomata, these tumours are not neoplastic, and have been called ' ecchordoses physaliphoræ '. In the same year Stewart gave this description of ecchordoses : " They are soft, transparent, jelly-like nodules attached by a more or less slender pedicle to the middle of the dorsum sellæ. They project through an aperture in the dura mater and often become loosely attached to the pia arach-noid covering the pons. They are in no sense infiltrative, and cannot be said to show any evidence of active growth."
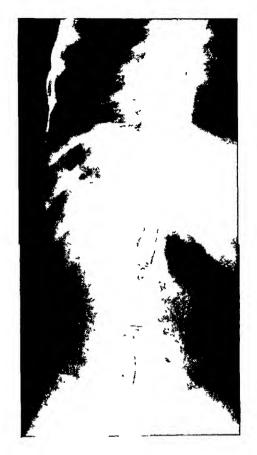
The tumour to be described, growing from a thin pedicle in the theca, suggests an origin from one of these ecchordoses physaliphoræ. But whereas ecchordoses are very soft, colourless, and transparent, this tumour was firm, purple, and translucent.

CASE REPORT

HISTORY.—Elsie C., 8 years of age, was admitted into hospital on Jan. 8, 1934, complaining of pain and stiffness of the back. Four months previously she had had a heavy fall on to her back, but it did not necessitate rest in bed. She had subsequently had pain in the thighs, mostly at night. Shortly before admission she had pneumonia.

ON EXAMINATION.—The child was seen to be pale and in poor general health, with wasted musculature. The back showed a very marked left-sided scoliosis, with rotation involving the whole of the dorsal and lumbar spine. On standing the scoliosis could be made to disappear, and was apparently due to spasm of the spinal muscles on the right side. Hips and knees were normal, with no individual

muscle weakness and no tenderness or neurological signs.   Standing and move-
ments of the spine caused pain in the right thigh.

A provisional diagnosis of tubercu-
losis of the dorso-lumbar spine was
made, but a series of X-rays showed no
bony lesion.

Feb. 17.—Mantoux and von Pirquet
tests were negative, but the child was
kept under observation for another three
months, there still being pain and rigid-
ity in the dorso-lumbar region, particu-
larly on the left side. Examination
under anæsthesia revealed nothing ab-

FIG. 14—Shows that the block extends
from the top of L 2 to the middle of L 4, where
the lipiodol appears to be partially surrounding
a nodule   The thecal obstruction is transparent
to X rays

normal in the abdomen, and the blood-
count was normal.

May 25.—The left knee-jerk and
ankle-jerk were found to be exaggerated,
while the left plantar reflex was extensor.
The right side was normal.   Sensation
in the left lower limb was normal.

May 28.—Lumbar puncture yielded
5 c.c. of straw-coloured fluid, the pressure
at first being high, but falling rapidly
until no further fluid was obtained.
Report on cerebrospinal fluid :—

Proteins ..	..	..	3 grm.
Chlorides	..	..	672 mgrm. per 100 c.c.
Sugar ..	..	..	60 mgrm. per 100 c.c.
Lymphocytes	..	..	8 per c.c.

June 1.—Lumbar and cistern punctures were performed, with injection of
light and heavy lipiodol respectively.   X-ray shown in *Fig.* 14.

OPERATION (June 16).—Laminectomy was performed, and the laminæ of L2,
3, and 4 removed.   The dura was found to be bulging, and a dark-coloured tumour
could be seen through it.   The dura itself appeared normal.   The appearance on
opening the dura is shown in *Fig.* 15.

The tumour was purple and lobulated, and appeared gelatinous.   Its only
attachment was a slender thread from its caudal part running down towards the
sacral theca.   This was crushed and divided, and the tumour removed, without
injury to the cauda equina.

The child made an uneventful recovery.

SUBSEQUENT HISTORY.—

July 2.—There was no pain or spasm, no symptom. Sensation normal. Reflexes :—

		R. Extensor	L. Flexor
Plantar		nil	+ +
Knee-jerk	..	nil	+
Ankle-jerk	..	nil	+
Abdominal	..	+	+

Sept. 7.—The child was walking normally with no symptoms. The right plantar reflex was still extensor, and the tendon reflexes were diminished on the right side.

Oct. 12.—As above.

I have been unable to correlate the neurological findings either with the original site of the tumour or of some subsequent recurrence.

PATHOLOGY. — On naked-eye examination the tumour was encapsuled, smooth and lobulated, purple in colour, and translucent (*Fig.* 16). It measured 4 cm. in length, 2·4 cm. in width, and 2 cm. in thickness. No large or well-defined blood-vessels were detected entering the growth. Near its lower pole, which consisted of a rounded lobule, was its pedicle. This was a white thread, about 1 mm. in diameter—that is, about the size of the nerve-roots of the cauda equina. The pedicle ran downwards and forwards towards the sacrum, but its origin was not determined.

MICROSCOPICAL APPEARANCE. — The capsule of the tumour is thin and fibrous. In parts it is œdematous and separated from the tumour by small extravasations of blood.

FIG 15 —Appearance on opening the dura

From it narrow fibrous trabeculæ containing numerous blood-vessels divide the tumour into lobules.

The cells forming the growth are epithelial in type and are arranged irregularly. In some parts (*Fig.* 17 *a, c*) they are closely packed in sheets with little or no intercellular substance, while in others they are in narrow trabeculæ, tubes, short strands, or even single cells separated by much mucinous material, and there

are all grades of variation between these extremes. In shape they vary from long spindles to polyhedra and spheroids. In the more cellular parts the protoplasm is uniformly stained by acid dyes. Everywhere, however, a certain number of vacuolated cells can be seen, and in the less cellular parts they are very numerous. Some are very large, forming the so-called 'physaliphorous cells' typical of chordomata. Mucin is present only occasionally in these cells. A very small number contain a few globules of fat, but most of the vacuoles are unstainable. As this material was received already fixed in formol saline, any glycogen which may well have been present would have dissolved out in this fixative.

FIG. 16.—Naked-eye appearance of tumour (× 1½.)

The nuclei also vary considerably. In the more cellular parts they are oval and vesicular with well-marked nuclear membranes and poorly-staining chromatin network. Most contain an eosinophil nucleolus, while some have two nucleoli. A few cells have two nuclei and many are hyperchromatic. Only two mitotic figures were seen in a careful search of twelve sections. In the more mucinous parts the nuclei are smaller and stain darker, and in many cells they have disappeared. A few vacuolated nuclei have been seen.
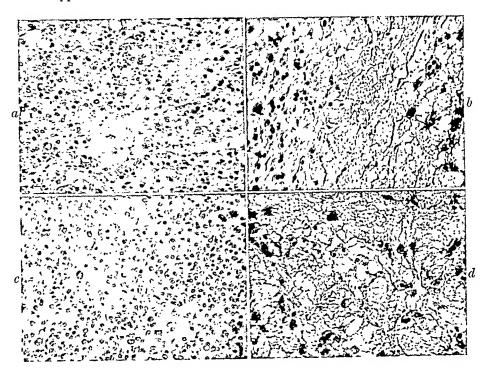
FIG. 17.—Microscopic appearance of tumour.

The mucin in this tumour is nearly all intercellular and is present in large amounts. As in Cappell's[5] *Case* 2 (1928) it is variable in its staining properties. With hæmatoxylin and thionin it is difficult to see, and mucicarmine and polychrome methylene blue will only stain it in parts. Toluidine blue demonstrated it most clearly, and the best metachromatic contrast could only be seen by examining the slide while wet in water. *Fig.* 17 *b* and *d* show typical mucinous areas stained in this way.

No " cord-like structures " (Cappell) or " nests of beakers " (Stewart) have been seen. There is no alveolar arrangement of the cells and only very few tubes, but nevertheless the cells are of frank epithelial appearance.

That the tumour is a chordoma seems certain for the following reasons : (1) Its situation within the theca growing on a pedicle as is usual with ecchordosis physaliphora ; (2) The purple soft jelly-like naked-eye appearance ; (3) The presence of typical physaliphorous cells and strands of cells with much mucin around them ; (4) The variability in the staining reactions of the mucin.

PROGNOSIS.—Chordomata are nearly always malignant tumours, and the cellularity, nuclear variation, and hyperchromicity as shown in *Fig.* 17 *c* make it unlikely that this is an exception. On the other hand, it is still surrounded by a capsule and was growing on a long pedicle, so that the chance of complete removal is good, and only time can show what the ultimate prognosis will be.

I have been unable to find any reference in the literature to a similar case. Chordomata occasionally invade the dura mater, but this tumour not only occurred in the lumbar region, which is exceptional, but also it appeared to be entirely intrathecal.

I am greatly indebted to Dr. W. D. Newcomb for his description of the histology of the tumour, for his excellent microphotographs, and his interest and help in this case.

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CARCINOID   TUMOUR   OF   A   MECKEL'S   DIVERTICULUM :
REPORT   OF   A   CASE

BY I. PRICE

DEPUTY MEDICAL SUPERINTENDENT, BETHNAL GREEN HOSPITAL, LONDON COUNTY COUNCIL

TUMOURS of a Meckel's diverticulum are extremely rare. In 1919 Symmers reported three cases of 'malignant myomata' of Meckel's diverticulum. Many cases of gastric and pancreatic heterotopia have been reported as occurring in relation to Meckel's diverticulum, but, so far as I am aware, only two other cases of carcinoid tumour of a Meckel's diverticulum have been reported in the literature. In 1922 Braxton Hicks and Kadinsky reported a case of a boy of 12 years of age who was operated on for supposed appendicitis. Laparotomy revealed a perforated Meckel's diverticulum. Braxton Hicks describes a section of his specimen as showing " in the submucosa, a strange mass of glandular tissue somewhat resembling shrunken pancreatic tissue though the arrangement is not pancreatic. This sub-mucosal glandular tissue has an appearance of 'splendid isolation' about it, for it does not resemble any tissue in its neighbourhood and it is apparently not connected by any gland, duct or structure with the mucosa beneath which it is situated. It does not penetrate into the deeper fibromuscular structures external to it." From this description and the diagram it appears that this is a case of pancreatic heterotopia without any suggestion of neoplastic formation.

A. L. Taylor and M. J. Stewart in 1926 described a case of carcinoid tumour of a Meckel's diverticulum removed post mortem from a man aged 54 years, who was dead on admission to hospital after collapsing in the street. They found at the tip of a Meckel's diverticulum a small tumour about the size of a pea. Micro-scopic examination showed it to be situated in the mucosa and the submucosa. " The muscularis was broken up and penetrated by columns and masses of tumour cells and on its outer aspect the growth had slightly invaded the muscular coat. Masson's silver stain revealed argentaffin granules in the basal portions of the peripheral columnar cells."

Stewart has come to the decision that Hicks and Kadinsky's case was not a carcinoid tumour, but really a case of pancreatic heteropia, and consequently Stewart's case is apparently the first reported in the literature.

In view of the rarity of the condition it was thought to be of interest to put on record an additional case.

CASE   REPORT

The patient, H. P., a married woman aged 54 years, was admitted to Bethnal Green Hospital on July 29, 1933, with a history of generalized abdominal pain since the day previous to admission. Persistent vomiting and diarrhœa had occurred. There was no history of a previous illness.

ON EXAMINATION.—The patient appeared toxic. The tongue was dry and furred. Pulse 92, respiration 32, temperature 99·8°. Urine normal. The abdomen was distended

and did not move on respiration. There was diffuse tenderness over the whole of the abdomen. No mass was palpable. Rectal examination was negative. Congestion of the lung was present.

OPERATION.—Laparotomy was performed on the same day as admission after a preliminary intravenous saline infusion. Gas and oxygen were given. A right paramedian incision was made. The peritoneum was inflamed, the pelvis contained a large amount of pus, the appendix appeared normal. About 2 ft. from the ileocæcal valve, along the small intestine, the omentum was found to be adherent. On gently dissecting off the omentum, a mass about the size of a small orange was found to be attached to the bowel. At the apex of the mass was a fibrous cord about the thickness of thick silk and about 6 in. in length which was attached at its other extremity to the posterior abdominal wall just below the mesentery. The mass was found to be fairly hard, and a diagnosis of an inflamed and an obstructed Meckel's diverticulum was made. A rapid resection of the bowel was performed with side-to-side anastomosis and the pelvis was drained.

POST-OPERATIVE COURSE.—The following day the temperature settled down to normal and the pulse-rate was 98. Vomiting was absent. The bowel remained confined. On Aug. 1, 1933, the abdomen became very much distended and vomiting became a marked feature. Efforts to cause the bowels to act were unsuccessful and it was evident that paralytic ileus had supervened. Injections of anti-gas-gangrene serum and saline infusion did not produce any improvement, and on Aug. 3 the patient died.

AUTOPSY.—A limited examination was made through the incision. The small intestine was found to be much distended. The anastomosis was sound. It was evident that the cause of death was paralytic ileus.

FIG. 18.—Photograph of specimen. a, Afferent limb; b, Efferent limb; c, Diverticulum.

EXAMINATION OF SPECIMEN (*Fig.* 18).—The specimen consists of a loop of intestine, one limb measuring 6 and the other 7 cm. in length. From the junction of the two limbs there projects an appendix-like diverticulum 5 cm. long, 2 cm. in diameter proximately, and 0·6 cm. distally.

On section through the specimen, the lumen of the intestine is shown to open by a narrow orifice in each limb into a cavity about 3 × 3 × 2 cm. This contains a little blood and some necrotic material. The wall of the intestine cannot be traced through the wall of the cavity, this being composed of milky white and pale yellowish tissue and measuring up to 1·5 cm. in thickness.

HISTOLOGY (*Fig.* 19).—I am indebted to Dr. W. Barnard, Histologist to the London County Council, for the microscopic description following : Sections were stained by hæmatoxylin and eosin, van Gieson, and Masson's stain. The tumour is composed of solid

trabeculæ and small acini composed of small polygonal cells separated in places by delicate strands of fibrous tissue containing blood-vessels, and in other parts by well-defined zones of fibrosis.

Similar strands and acini are present between the muscle bundles of the diverticulum. The central part of the tumour is necrosed, the cavity seen by the naked eye being necrotic
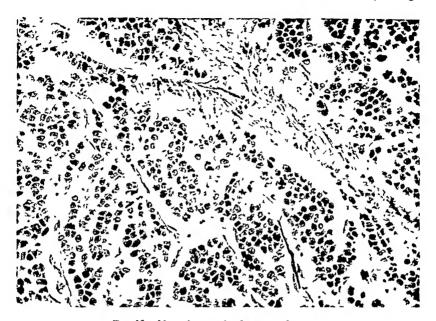
FIG 19.—Microphotograph of section of tumour.

autolysed tumour. In no part of the sections could granules be demonstrated in the cells, and the silver stain was negative.

DIAGNOSIS.—Solid trabecular and acinar polygonal-celled carcinoid of Meckel's diverticulum.

DISCUSSION

Carcinoid tumours are most commonly found in the appendix and have in the past been confused with carcinoma of the appendix. Stewart found 17 cases in 500 consecutive appendices removed between 1910 and 1924 in Leeds General Infirmary.

In 1838 Merling described the first case of carcinoma of the appendix. The first contribution to the subject of carcinoid of the small intestine was made by Lubarsch in 1888, when he described two cases, in one of which he found two small tumours, and in the other six small tumours, in the ileum. Lubarsch described these nodules as situated in the muscularis and the submucosa and composed of nests of cells and resembling somewhat adenocarcinoma occurring elsewhere. Though the cells were dissimilar and the tumours multiple, he found no metastases. Lubarsch called them 'primary carcinoma of the ileum.'

In 1890 Random described a tumour of the ileum similar to that of Lubarsch's, but in which he found secondary deposits in the liver.

Since this time many cases have been reported, some of them being only discovered at autopsy and in cases associated with appendicitis.

A. J. Kelly described four cases and called them 'endotheliomas'. It was Obendorf in 1908 who first applied the name of 'carcinoids' in contradistinction to the carcinomas. He based his conclusion on the following facts: (1) Tumours are often multiple; (2) Cells are undifferentiated, but may show glandular forms; (3) They do not form metastases; (4) They lie in the submucosa but may send processes into mucosa; (5) Muscularis mucosa is always present; (6) Stroma is smooth muscle derived from muscularis mucosa.

Frappe considered the carcinoids to be pancreatic 'rests', while Bunting regarded them as analogous to Krompecher's basal-celled tumours of the skin.

Hubrschman in 1910 suggested that the carcinoid tumours, because of their yellow colour, were derived from the 'gelben zellen' of the intestinal mucosa. Schmidt had previously established the chromaffin character of the 'gelben zellen'.

Gosset and Masson in 1910 applied the silver impregnation method of staining the chromaffin cells, and described them as: (1) Occurring in the depths of the crypts of Lieberkühn throughout the gastro-intestinal tract; (2) Occurring between the cells of the mucosa, some extending to the lumen and others not; (3) Showing argentaffin or silver staining granules in the cells; (4) Cells showing vacuoles in cytoplasm which are probably the results of elaboration of granules.

Gossett and Masson proceeded further, and they showed that the carcinoid tumour cells closely resemble and are identical with the chromaffin tissue of paraganglia which are filled with argentaffin granules. Masson regarded them as endocrine tumours because the medullary cells of the suprarenal exhibited micro-chemical similarities. Masson's researches have progressed still further, and in 1928 he showed in chronic cases of appendicitis the argentaffin cells derived from the Kulchitsky cells situated amidst the cells of the crypts of Lieberkühn had invaded the hyperplastic nerve plexus or musculo-nervous complex and that further development resulted in the formation of a carcinoid tumour.

Summary of Theories Concerning the Carcinoids.—The theories concerning the carcinoids may be summarized as follows: (1) They are carcinomas; (2) They are basalomas analogous to Krompecher's basal-cell tumours of the skin; (3) They are pancreatic rests. (4) They are chromaffinomas derived from the Kulchitsky cells of the crypts of Lieberkühn and therefore are tumours of the paraganglia.

Discussion on the Case Reported.—It will be noticed that the case reported does not stain with Masson's stain. On the other hand, it does not appear that the section is that of a pancreatic rest. It has not the appearance of 'splendid isolation' that we see in cases of pancreatic rest, and, further, the cells are definitely invasive in character. We can therefore assume, perhaps with reservation, that the cells may be more primitive in type than those of the fully developed carcinoid

SUMMARY

1. A short review of the literature on carcinoids is given.

2. The rarity of a carcinoid in Meckel's diverticulum is emphasized.

3. A case of tumour of a Meckel's diverticulum is reported, and it is suggested that the cells are of a primitive carcinoid type.

4. The pathology of the carcinoids is reviewed.

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INCISIONAL HERNIA*

By E. S. J. KING

SURGEON TO OUT-PATIENTS, MELBOURNE HOSPITAL

MANY ' causes ' of incisional hernia are given in text-books and current papers. Some of these—for example, the presence of infection, the use of drainage tubes, " too early adoption of the upright posture ", etc.—do not deal with a fundamental factor, and others ("inadequate formation of the cicatrix ", " giving way of the scar ", etc.) are but imperfect statements of one or other of the phenomena which are associated with and not causative in the development of the condition.

An attempt has been made here to show that the many factors which are regarded as causative may be reduced to terms of certain fundamental principles.

HISTORICAL

During the Middle Ages the various forms of abdominal hernia were not differentiated from each other. In 1585 Guido de Chauliac in his *Chirurgica Magna* distinguished umbilical hernia from those occurring in other parts of the abdominal wall. Further observations were made, amongst others, by La Chausse in his *Dissertation de Hernia Ventralis* in 1746, and by Klinkosch in 1764.

It was only at the beginning of the last century, however, that attention was attracted generally to the ventral herniæ. A ventral hernia was described as a protrusion " through an unnatural opening in the front or side of the belly ". At this time the majority of ventral herniæ were those through the linea alba and the linea semilunaris. A few cases following wounds by knives, sabres, bullets, etc., were encountered. In Chelius' *System of Surgery*, translated by South in 1847, it was stated that ventral hernia " is much more rare " than umbilical hernia. At this time post-operative rupture is not mentioned.

As abdominal section became more common it was found that herniæ through the scars were occurring in considerable numbers. In 1893, in his *Treatise on Ruptures*, Jonathan Macready remarked, " It is not now uncommon to find a traumatic hernia after the operation for Ovariotomy ".

Despite improvements in technique, in asepsis, in anæsthesia, and post-operative treatment, hernia after operation still remains a serious problem.

CLINICAL CHARACTERISTICS

Incisional hernia is here referred to as the protrusion which occurs through the site of a wound, and is not intended to include those cases in which a bulging

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* Since writing the above I have observed an account of the development of incisional hernia (Freeman, L., " Cause of Post-operative Rupture of Abdominal Incisions ", *Arch. of Surg.*, 1927, Feb., 600) which contains a consideration of the problem from a somewhat different aspect. On the fundamental point, however, there is agreement.

occurs as the result of loss of tone or degeneration of muscle following injury to nerves. It arises through any of the incisions which are made in the abdominal wall—most frequently in the lower portion of the abdomen. In 150 consecutive cases it was found that post-operative hernia occurred through a sub-umbilical mid-line incision in 30 per cent of cases, muscle-splitting (McBurney) incision in 27 per cent, sub-umbilical paramedian incision in 14 per cent, and supra-umbilical paramedian incision in 14 per cent. There is usually a latent period between the time of operation and the development of the hernia. This may be very short, only two or three weeks, or several years may elapse before the observation of a pulsatile swelling under the scar.

Table I.—Interval Between Operation and Development of Hernia in 150 Cases

Time between Operation and Development of the Hernia	Number of Cases	Percentage
0–4 weeks	61	40$\frac{2}{3}$
1–3 months	15	10
3–6 months	19	12$\frac{2}{3}$
6–12 months	18	12
1–2 years	12	8
2–5 years	7	4$\frac{2}{3}$
5–10 years	6	4
10–20 years	3	2
Over 20 years	1	$\frac{2}{3}$
Not given	8	5$\frac{1}{3}$

It will be seen from *Table I* that the majority of the cases were observed shortly after the operation, usually when the patient was allowed out of bed. This observation may be the reason for the opinion that too early assumption of the erect attitude is responsible for the development of such herniæ. When allowance is made for the obesity of many of the patients—which makes early observation difficult—and also for the fact that in many cases the first observations are made by the patients themselves, so that any abnormality of mild degree is probably overlooked for some time, it is apparent that the great majority of the cases occur almost immediately after the operation.

As shown in *Table I*, 40 per cent of the herniæ develop within a month of operation, i.e., they are present when the patient gets out of bed ; 50 per cent are present within three months, 63 per cent within six months, and 75 per cent have become obvious within a year. On several occasions I have examined a scar and discovered a hernia of which the patient was quite unconscious, so that most of these periods should probably be shortened in order to gain a real idea of the time of development of the condition. Incidentally in some cases the patients had ' no idea ' of the length of time that the hernia had been present (last group).

Some of the cases seem almost certainly to be late developments and due to a tearing of the peritoneum at a late stage; e.g., in the case in which the hernia developed over twenty years after the operation (twenty-six years), the patient noticed a swelling after a severe abdominal strain associated with pain in the scar. Three other cases, with 8-year, 12-year, and 15-year intervals, all experienced injuries or strains which gave rise to pain in the wound. Several of the cases

occurred during the late stages of pregnancy or parturition; one who showed a 5-year interval gave birth to twins just before noticing the hernia.

It is almost impossible to decide in these cases whether there is actually a tearing of the scar tissue or whether there had been a latent hiatus in the scar (filled with omentum) all the time. Inasmuch as on the one hand the latter may remain latent, and on the other scar tissue is very firm and strong, the second hypothesis seems more likely even for the late cases. The increased intra-abdominal pressure therefore causes a rapid increase in size in the original small herniation.

When the hernia is first observed it is often a typical protrusion of intra-abdominal contents through the wall, more or less reducible, and giving a definite impulse on coughing or straining. When observed at an early stage of its development, however, it may not be reducible or show an impulse on coughing. It may be mistaken for a small hæmatoma, more or less organized. Later it develops the characteristic features of the well-developed condition.

The hernia, if allowed to develop without interference, gradually becomes larger and larger; some very large examples may be encountered, but this is unusual, since the life history is cut short by obstruction of the gut.

The neck of the sac is often found to be relatively small, and often there is more than one opening through the abdominal wall.

SURGICAL ANATOMY

The hernia is usually irregularly ovoid or rounded in shape, showing a number of loculations. It is covered by a layer of fibrous tissue, fat, and skin. Sometimes
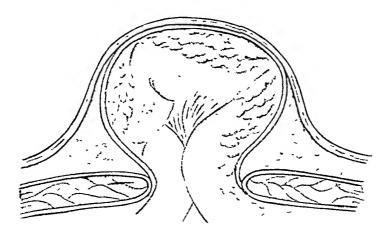
Fig. 20.—Diagrammatic representation of an incisional hernia which contains small bowel and omentum.

the cavity comes into close proximity with the skin, and the sac may be adherent to it.

The neck is a firm fibrous ring, which is usually much smaller than would be expected from a clinical examination of the hernia before operation. If the hernia is reducible, even partially, the dimensions of the neck may, of course, be determined before operation.

The septa separating the loculi in the sac project for varying distances into the cavity (*see Fig.* 21), and some may extend so far as to divide the opening at
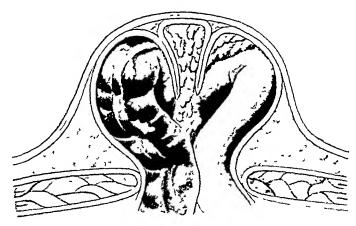

FIG. 21 —Diagrammatic representation of an incisional hernia which contains large intestine, omentum, and small intestine. Septa which partially subdivide the hernial sac are shown

the neck, i.e., the neck consists of more than one opening into the sac. The sac is lined by a serous layer which is thinner and more tenuous in appearance than normal peritoneum.

The contents of the sac may be omentum only or omentum and bowel, either small or large intestine or both (*Figs.* 20, 21). The contents, particularly

FIG 22 —Drawing of the peritoneal aspect of scar tissue removed from the site of an old operation   Multiple openings which had contained omentum are shown.   These strongly suggest the escape of omentum between sutures.

FIG. 23 —Drawing of the peritoneal aspect of tissue removed in a case of incisional hernia In addition to the large opening (sac shown behind) there are other smaller openings (cf. Fig. 22).

the omentum, are usually adherent at various places to the wall of the sac.   These 'adhesions' are slight and tenuous in some cases, but are often dense and thick,

containing dense fibrous tissue.   The ' adhesions ' are significant from the point of view of the mode of development of the hernia, and are discussed again.

In some cases there are separate openings in the scar for a number of small distinct herniæ.   These may be well demonstrated at times when the scar tissue has been removed completely.   This is shown in *Figs.* 22, 23.

HYPOTHESES OF THE MODE OF FORMATION OF INCISIONAL HERNIA

A number of different factors are regarded as being causative.   Some of these —use of a drainage tube, suppuration, or raised intra-abdominal pressure—are, or have been, present, but do not supply the explanation of the mode of formation. " Inadequate formation of the cicatrix ", " giving way of the scar ", " poor healing " are only indefinite statements of opinion—statements without any basis of direct observation for their support.   " The too early adoption of the upright posture " is even more nebulous, since this involves a number of fundamental conditions such as alterations of intra-abdominal pressure, the mechanism and rate of healing, etc.   From my own experience I would regard it as playing but little part in the development of hernia.   " Imperfect technique " is undoubtedly the cause of many cases, but a statement of exactly where the technique is unsatisfactory is necessary.
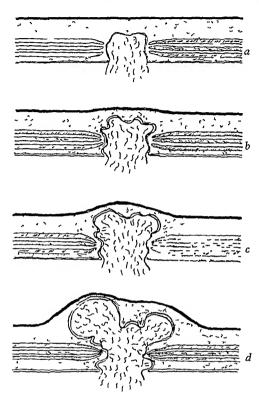
A number of observations on early cases, the multiple loculations, the frequency of adhesions, the difference in the appearance of the lining of the sac of the hernia from ordinary peritoneum, all suggested that the sac did not arise by the pulsion of peritoneum through a weak area of the wound by the pressure of the intra-abdominal contents.   The observations were then reviewed in the light of the hypothesis that the sac is secondarily formed.   Animal experiments were undertaken.

Experimental Material.—Cats were taken and ventral herniæ produced. A mid-line incision into the abdominal cavity was made under general anæsthesia, and the skin then separated from the obliquus abdominis externus for a considerable distance laterally.   A small opening was made in the abdominal wall in the lateral part, and omentum was passed through into the subcutaneous tissues.   One part of it was tethered by a catgut suture.   In some cases a loop of small intestine was also passed through the opening and tethered.   (Plain oo catgut was used.)   The mid-line wound was then closed in layers.   Except for one cat in which suppuration occurred in the wound, and two others in which intestinal obstruction in the hernia supervened before the sixth day, the animals made an uninterrupted recovery.

At first a firm mass could be felt in the region of the prolapsed omentum. There was no impulse when the animal struggled.   The wounds healed and the condition of the swelling remained stationary until at a variable time later (seven days in one cat, fourteen days in another, but on an average about ten days) the mass was found to show an impulse when the animal struggled.   This gradually became more obvious until there was a typical hernia.   One hernia became smaller in size and finally almost reduced itself completely, only a small amount of additional tissue being felt in the subcutaneous layer.   Two others became much larger, but the majority remained about the same size.*

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* This is possibly to be correlated with the relative infrequency of herniæ in quadrupeds. Also the animals were observed only for quite short periods.

The animals were sacrificed at different times after the operation (five to twenty-eight days). The anterior abdominal wall containing the hernia was removed and the omentum and gut (where present) passing into the hernia were cut at a distance from the abdominal wall. The hernia was then dissected.

In the early examples (five to ten days) the omentum and bowel were found to be adherent to the surrounding connective tissue. This could be separ-

FIG 24 —Diagrammatic representation of the mode of development of the sac of an incisional hernia a, Prolapsed omentum, b, Small serosal cavities forming in part from the serosa of the omentum and in part by ingrowth from the peritoneum, c, Further stage of b, d, Enlargement of the hernia and coalescing of adjacent serosal spaces

ated readily by sharp dissection or by a blunt instrument with tearing of the adhesions. No cavity could be found round the omentum. In the later cases, and usually in those in which pulsation had been present when the animal struggled, small cavities separating the omentum or bowel from the connective tissue could be found (i.e., small serous spaces). These were best developed in those examples which were investigated the longest time after operation (*Fig.* 24).

FIG 25 —Photograph of specimen of a hernia, viewed from peritoneal aspect, showing omentum entering the sac (sixteen days). The neck is well demarcated
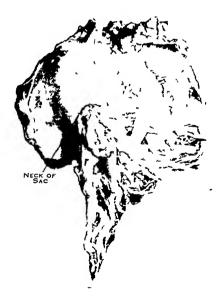

NECK OF SAC

The cavities were small and separated from each other by bands or areas where the hernial contents and the wall were still adherent. In some examples the cavities were near the entrance to the abdomen and appeared to communicate with the abdominal cavity. The neck of the hernia was usually well marked (*Fig.* 25).

The demonstration of the independence of some of the serous cavities from each other and the continuity of some with the peritoneum was performed as follows : Herniæ were produced (as above), and after five to six weeks, under anæsthesia, a solution of methylene blue was injected into the abdominal cavity. This was massaged into the region of the hernia. The hernia was now examined after removal of the skin over it, from the superficial aspect. Some of the loculi of the sac were obviously distended with the blue fluid, while others were found on dissection not to be stained. Comparable uninvolved loculi were injected with carmine gelatine and it could be seen that (1) they did not communicate with the ' blue ' loculi, and (2) they did not all communicate with each other. Some diffi- culty was encountered in placing the injection within the serous cavities, but by trial and error (injection was sometimes commenced into tissue planes, but this was early recognizable and proved later on dissection) injection of a number of cavities was made (*Fig.* 26). However, even without this the freedom of certain
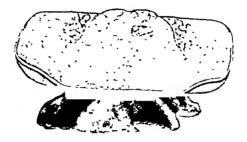

FIG. 26.—Drawing showing the loculi of a hernia filled with dye. The peritoneal surface and intraperitoneal contents are stained blue, and some of the loculi in the sac are blue. Other loculi are stained with carmine.

loculi from the blue coloration in the first experiment seems to be a satisfactory demonstration of their separation. This was controlled by attempting to force the carmine into the abdominal cavity. This was achieved with ease by injecting a ' blue ' loculus, but could not be performed even by bursting other loculi. Two deductions may be drawn from this :—

1. Since certain of the loculi are formed away from the peritoneal lining near the neck of the sac, and are not in communication with it, the endothelium (or mesothelium) lining such loculi must have arisen from multiplication of the serosa of the omentum or bowel. After this multiplication, splitting of the cellular (mesothelial) tissue probably occurs so that each side now possesses a lining. Attempts were made to demonstrate this histologically, but a completely convincing picture was not obtained.

2. The fibrous bands or areas which separate the various loculi are, on dissec- tion, closely similar to the ' adhesions ' found at operation.

Since within the limits of these experiments these adhesions become fewer in number and less well marked as the condition progresses, it is assumed that they are the residue after partial ' peritonealization ' of the hernia. It is possible that the sac is at first formed and then secondary adhesions arise, but no evidence of inflammation of the bowel was to be seen. Almost certainly such inflammatory and secondary adhesions occur in human beings, but at least in the early stages the method of formation of the ' adhesions ' described above seems probable.

In some cases either the various loculi become continuous with each other or all the serosal lining is developed from one origin (possibly the peritoneum), because rarely the whole sac may be free from ' adhesions ' and the contents lying free within it.   This was found in one cat, in which the hernia was examined at the end of a month.

DISCUSSION

As with so many other conditions encountered in surgical practice, the incisional hernia is most commonly observed in a well-developed form which is actually the end-result of changes the nature of which can only be conjectured.   The evidence nevertheless, though only circumstantial, seems to point in a definite direction.

The anatomical features of the developed hernia, particularly the relatively large size of the sac in many cases as compared with the opening in the wall, indicate that the factors are definitely localized to one point in the wound.   Thus a " giving way " or " stretching " of the scar does not explain these cases.   In the examples where there are multiple openings (*see Figs.* 22, 23) the same argument applies, since these openings are quite distinct from each other and separated by bands or sheets of ordinary scar tissue—i.e., the factors are still acting locally, though in more than one place.

The problem is :   What factors cause or allow the local protrusion of the abdominal viscera ?   Omentum or even bowel will pass very readily into any small hiatus which is left between sutures.   On one occasion, three days after operation, a small knuckle of bowel was found in the tissues of the anterior abdominal wall. The cause appeared to be the cutting, or at least the laceration, of the catgut peritoneal suture by the cutting-edged needle on which the silkworm-gut sutures were threaded.   In another case a small piece of omentum had prolapsed through the small opening made by the passage of a bullet (*Fig.* 27).

The difficulty in preventing a small piece of omentum from entering the wound when this is being sutured, particularly when anæsthesia is difficult or incomplete, is shown by the many methods suggested for preventing this.   Careful observation of operations at this stage, incidentally when most onlookers cease to take interest, shows that small pieces or tags of omentum are sometimes included in the wound between sutures.   This suggested the experimental work undertaken, and the similarity of the clinical course of the experimentally produced herniæ with some post-operative ones suggests that this is the actual mode of formation.

The observation that so many of the cases have a hernia when they are allowed out of bed also strongly suggests that some such mechanism of formation occurs. If this is so, then at least some of the cases are due to error of technique—i.e., intra-abdominal contents, usually omentum, are allowed to escape into the extra-peritoneal tissues.

Others, however, do not fall into this class.   The commonest cause of hernia is infection.   The mode of development here is associated with early solution of portion of the catgut and the delayed healing of the wound.   This may be readily observed in those cases when it is necessary to re-open the wound two to four days after the operation.   This disappearance of the catgut prematurely gives a condition of affairs similar to that seen in the previous group of cases.   Some degree of intestinal distension is often present and a small amount of omentum or bowel passes into the wound.

Debilitating conditions—e.g., carcinoma—are recognized as delaying healing. I have seen, after the removal of sutures in such a case, the wound open as late as the twenty-first day. The solution of the catgut before healing has occurred will allow the passage of omentum into the wound. This, therefore, also may be correlated with the first group. Such cases are closely related to those of "disruption of an abdominal wound" or "burst abdomen", the difference between these and a hernia being largely a question of degree of protrusion of the viscera into or through the abdominal wall.
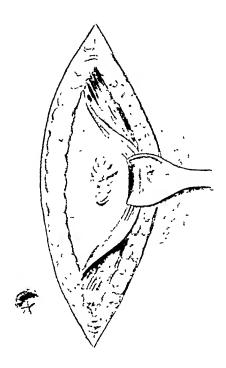

FIG. 27.—Drawing of an abdominal wound (left upper paramedian) showing the prolapse of a piece of omentum through a bullet hole. The bullet wound had occurred two hours before operation.

Raised intra-abdominal tension is, of course, a factor in the production of hernia in so far as it will facilitate the protrusion of omentum or bowel, but its importance is secondary to the integrity of the suture line.

The adoption of the upright posture does not seem to me to be a primary factor in the development of the condition, which depends on the presence of a hiatus in the wound.

Once the condition has commenced, omentum having entered the wound, formation of the sac will occur, and this will then gradually become larger. The

early development of a non-pulsatile swelling which later becomes pulsatile, as mentioned above and observed in the animals, strongly supports this mode of formation.

From a consideration of the above, certain principles of technique appear. These are more or less generally recognized, but emphasis may not be out of place. No hiatus must be left in the suture line, and no tissue—particularly omentum—even in the smallest amount, must be allowed between sutures. Through-and-through sutures, if closely placed and no omentum prolapses between them, will give a satisfactory wound which will not be followed by hernia in any greater proportion than in those in which other methods are used. I have had occasion to re-open, several months after operation, a number of cases in which through-and-through sutures were used, and found that the various layers of the abdominal wall could be demonstrated as if they had been sutured in layers. Small tears in the peritoneum such as sometimes occur when there is some straining of the wall are just as dangerous as openings between the sutures. These may be avoided by the use of through-and-through sutures.

Drainage tubes and wound infection present difficult problems. Having seen herniæ develop in two of my earlier cases through a muscle-splitting incision, I have since made it a practice to bring the tube through a stab incision, thus allowing complete closure of the wound. Where infection of the wound is probable —e.g., in an appendiceal abscess—swabbing the wound with sterile vaseline or bipp before opening the peritoneum greatly diminishes the incidence of wound infection.

CONCLUSIONS

The essential feature in the development of an incisional hernia is the escape of some of the contents of the abdomen (usually a small piece of omentum). This may occur through a small tear in the peritoneum or through a small hiatus between sutures. In the case of infection, the early solution of the catgut may allow the escape of omentum. The sac is formed secondarily round such tissue and may then become larger and show the characteristic phenomena of a pulsatile hernia. The adhesions so frequently found in these herniæ are not secondary adhesions, but are due most frequently to the localized rather than the completely generalized formation of the secondary sac.

POSTERIOR SEGMENTAL BLOCK-EXCISION OF THE BLADDER NECK WITH PRIMARY CLOSURE

By S. HARRY HARRIS

HONORARY UROLOGIST, LEWISHAM HOSPITAL, SYDNEY

THE operation of posterior segmental block-excision of the bladder neck with primary closure is presented in the belief that it is an improvement on the well-recognized operations of cuneiform (or wedge) resection and of complete extirpation of the bladder neck ("*ablation totale du col*" of Marion). The first-named operation is too liable to be followed by recurrence of the obstruction. The latter operation, while yielding apparently excellent results according to the reports of its sponsors, is open to the objections that it is needlessly extensive and that it leaves a wide-open raw surface, the bleeding from which is controlled by gauze packing (Marion[1]).

The operation devised by the author, and herewith described, has been practised by him thirty-three times in the past six years without mortality and, up to the present, without recurrence of obstruction. It may be regarded as a companion to the author's operation of suprapubic prostatectomy with closure.

The operation is designed for the relief of certain obstructive conditions of the bladder neck when no gross enlargement of the prostate is present, the "*prostatisme sans prostate*" of the French. These conditions include the various types of median bar formation or disease of the posterior commissure and general prostatic fibrosis. The operation has no place in the treatment of lateral lobe enlargement of the prostate, though it will prove of value in some cases where the bladder has to be opened for the treatment of recurrence of obstruction after prostatectomy.

The tissue removed at operation may prove to be fibrous, adenomatous, or muscular, alone or in various combinations, or occasionally even carcinomatous.

The operation is undertaken only after definite proof is forthcoming that there is present no adenomatous tissue in the prostatic rim which is capable of digital enucleation. To ensure this a careful bimanual palpation is carried out with the forefinger of one hand placed in the previously dilated prostatic urethra, and the forefinger of the other in the rectum. To remove an obstructing posterior lip and to leave behind adenomatous tissue elsewhere in the prostate is merely to court future trouble. This, of course, constitutes an essential weakness in the per-urethral methods of operation.

Per-urethral resection will, however, still be the method of choice in dealing with some forms of obstruction of the bladder neck when no gross enlargement of the prostate is present; in others the trans-vesical approach will be considered preferable. In making the selection due regard must be paid not only to the actual obstructive condition of the bladder neck, but also to the presence of possible complications such as calculus or diverticulum of the bladder, gross hypertrophy

of the inter-ureteric bar, and the like. The author's experience during the past six years is about evenly divided between the two methods. He is at present decidedly of the opinion that in the long run the trans-vesical operation herewith described will more than hold its own with the per-urethral methods of resection both as regards immediate safety and, more particularly, for permanence of results. In either case the pre-operative treatment will be the same as for prostatectomy.

OPERATIVE TECHNIQUE

After exposure of the bladder base by the same technique as the author employs for prostatectomy, the tip of the right forefinger is gradually but firmly insinuated through the internal meatus. The very dense, infiltrated bladder neck with contracted meatus, so often present in the type of case under review (*Fig.* 28), not uncommonly declines to

FIG. 28.—Showing the indurated contracted meatus often found in disease of the bladder neck, and hypertrophy of the inter-ureteric bar.

yield to any but the firmest and most persistent pressure. Two fingers of the left hand are passed into the rectum and provide an invaluable point of counter-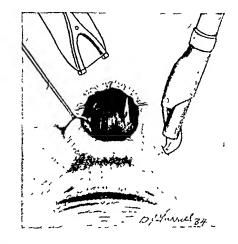pressure during this manœuvre. This preliminary dilatation is very important and greatly simplifies the subsequent steps of the operation.

Two deep traction sutures are now placed in position, one on each side about half-way round the dilated prostatic rim (*Fig.* 29). Following this, at least $\frac{3}{4}$ in. of the hindmost sector is excised (*Figs.* 30–32). In order to carry out this excision two deep parallel vertical incisions are made, one on each side of the mid-line and reaching in the depths down to the level of the floor of the prostatic urethra
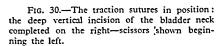
FIG. 29.—The same case as *Fig.* 28, after digital dilatation of the meatus. The left lateral traction suture is in position. The boomerang-needle is ready to receive the right lateral suture from the ligature carrier. The ready access afforded by the preliminary dilatation is well shown. The slight lacerations resulting from the dilatation are indicated.

(*Fig.* 30). The intervening lip is then firmly drawn up by traction forceps and cut out deeply and cleanly in a transverse direction by sharp scissors (*Fig.* 31). The bared base (*Fig.* 32) must be carefully reviewed, and, if need be, trimmed up. It is important that no gross fibrous or adenomatous remnants be left in

this situation. The cross-cut ends of the prostatic rim are next freely undercut on each side to permit of their complete retraction (*Fig.* 33 and inset). Two deep hæmostatic sutures are then passed on each side behind the two traction sutures that were inserted prior to the excision. These sutures also serve to
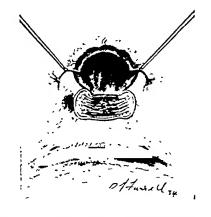

FIG. 30.—The traction sutures in position: the deep vertical incision of the bladder neck completed on the right—scissors 'shown beginning the left.

FIG. 31.—Vertical incisions complete. Block-excision in progress.

FIG. 32.—Block-excision completed, showing fibrous bands running from the cross-cut ends to the floor. These are a potential source of recontraction when left behind.

turn in on each side the bared face, of the cross-cut ends, thus eliminating the raw surface in this situation (*Figs.* 34–36). If necessary one or more additional sutures are placed to ensure complete hæmostasis. When hæmostasis has been accomplished, retrigonization is carried out. This step, which the author first

described in the operation of suprapubic prostatectomy with closure, is of equal value here. Retrigonization is the name which the author has applied to the method of sewing down the apex of the trigone into the prostatic urethra, its normal habitat, in order to ensure freedom from post-operative ledge formation
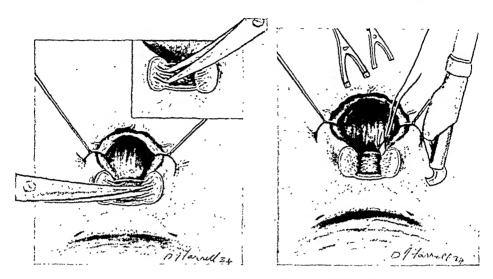

FIG. 33.—Undercutting of the cross-cut edges.

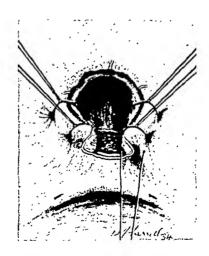FIG. 34.—Insertion of first hæmostatic suture on the right behind the original traction suture.

FIG. 35.—First right and left hæmostatic sutures tied, second right lateral hæmostatic suture in position before tying. The tying of this suture turns in the cross-cut edges and obliterates the raw surface in this situation.

after prostatectomy (Harris[2]). The point of the needle for this step (*Fig. 36*) penetrates the bladder base at the deepest part behind the inter-ureteric bar, following the author's latest practice (Harris[2]).

Retrigonization completes the plastic portion of the operation (*Fig.* 37).   The anterior obliterative sutures which are employed after suprapubic prostatectomy are not required for this operation, as the anterior segment of the bladder neck has not been interfered with and there is no raw surface left to obliterate.
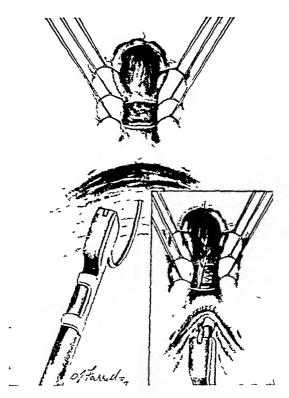

FIG 36—Lateral sutures in position, hæmostasis complete   Retrigonization begun   the point of the boomerang-needle is about to penetrate the deepest part of the bladder base well down behind the trigone   *Inset*   The point of the needle emerging in the prostatic urethra ready to receive the suture

FIG 37—Retrigonization complete   the apex of the trigone sewn well down into the prostatic urethra   All raw surfaces obliterated
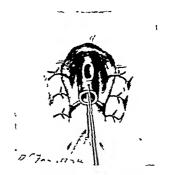

FIG 38—Catheter in position ready for complete closure of the bladder

A number 22 French rubber catheter is passed through the urethra into the bladder, and its end, including the eye, is cut off after an opening has been cut about an inch behind the eye. The catheter is suspended in position by a silkworm gut suture (*Fig.* 38). The bladder and abdominal wounds are completely closed and the silkworm gut suture is suspended to a small glass rod on the abdomen according to the author's practice after prostatectomy.

The after-treatment is the same as that employed after prostatectomy.

SUMMARY

1. A new operation is described for the treatment of obstructive disease of the bladder neck in which there is no gross enlargement of the prostate. It may be regarded as a companion to the author's operation of suprapubic prostatectomy with closure. It has been carried out thirty-three times without mortality.

2. The operation described eliminates the liability to recurrence of obstruction which characterizes cuneiform resection.

3. The operation is less extensive and safer than complete extirpation of the bladder neck ("*ablation totale du col*" of Marion) and should ensure results at least comparable with those claimed for this operation.

4. The diseases for the treatment of which this operation has been designed will often be treated by per-urethral resection, though with what degree of permanence yet remains to be proved.

5. The type of operation selected should be determined not only by the particular local obstructive condition of the bladder neck but also by the incidence of such complications as stone and diverticulum of the bladder.

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[1] MARION, G., " Maladie du Col vesical ", *Trans. Fifth Congress Internat. Soc. of Urol.*, 1933, July 11–15, 393.

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A CASE OF HYPERINSULINISM RELIEVED BY PARTIAL PANCREATECTOMY

BY J. ALLAN BERRY

HONORARY SURGEON, NAPIER HOSPITAL, NEW ZEALAND

SINCE the clinical picture of insulin shock from overdosage (hyperinsulinism) has become generally known, some hundreds of cases of spontaneous hypoglycæmia have been reported in the literature. The condition is associated with a variety of clinical syndromes and there can be very little doubt that when the less severe cases of the malady become generally recognized it will be found to be a relatively common complaint. Those cases caused by an adenoma of the pancreas have lent themselves to surgical treatment with excellent results, but those cases where the pancreas appeared normal and where partial pancreatectomy has been carried out have, up to the present, been unsatisfactory. Wauchope[1] states that " Partial resection of a normal pancreas does not seem worth while." The opposite view is held by Wilder,[2] who made the confident prophecy : " The situation is analogous to that of the early history of surgery in hyperthyroidism. The results in this new field ought to be as good as those obtained in hyperthyroidism, and I predict they will be." Best,[3] on the other hand, states, " While it is possible, as has been suggested, that a small tumour might escape attention, it is by no means clear that the history of the development of the surgical treatment of hyperthyroidism will be repeated in this instance." After mentioning the rational treatment of these cases (1) by supplying carbohydrates, (2) by stimulating new production of carbohydrates as by thyroxine, (3) by the surgical removal of a tumour should it be present, he states, " To this list there may shortly be added the use of a potent diabetogenic substance prepared from the anterior pituitary. If, as may well be the case, the therapeutic effects of the extract from the anterior lobe are not satisfactory, the clinician will probably be forced in severe cases of spontaneous hypoglycæmia to recommend excision of a large part of the pancreas, irrespective of whether or not the presence of an adenoma is suspected."

The object in reporting the following case is to show that when a sufficient amount of normal pancreas is removed, alterations take place in the blood-sugar which persist for some months, and the condition of hyperinsulinism may be relieved.

CASE REPORT

Miss A. M., a school teacher, aged 58 years, was first seen on Dec. 8, 1933, following a hypoglycæmic attack.

HISTORY.—The patient's father died from "natural causes" at the age of 89 years, and her mother of " peritonitis " at the age of 86 years. There was no family history of diabetes or glycosuria. Two sisters suffer from attacks that may be due to spontaneous hypoglycæmia.

At the age of 11 years she had a severe attack of measles and at the age of 12 mild diphtheria. Apart from symptoms referable to the present condition, she had suffered from no other
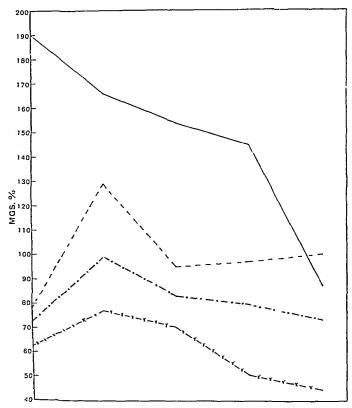
illness except from what was diagnosed as rheumatic fever ten years ago, when she was off duty for five months. The menopause had occurred at 51 years and was symptomless.

The first attack of vertigo, which was her outstanding complaint, came on suddenly about fourteen years ago while in a cinema. Next morning on waking she was still a little dizzy. Some time later another attack of dizziness occurred, when she vomited freely. Shortly after this, in her own words :—

" I was awakened at about 4 a.m. daily and would find my hands resting on my stomach, and on removing them, this awful depressing feeling of being thoroughly ill would pass off and then I would vomit quietly as if the stomach revolted from food. I would sleep then, till time to arise. My breakfast consisted of a cup of tea and a granose biscuit. Sometimes I was not too steady on my walk of nearly two miles to school. This gradually increased until I became very unsteady in my gait and often used to stagger in places and had to keep my eyes ' front ', not daring to look sideways. Then came dizzy turns at school, where I would sit quietly for half an hour or so and then go out and vomit. This would give relief, and I would then be able to go on for the rest of the day. These school turns became very frequent. This is now about twelve years ago. By this time I had found that starvation would relieve me, and that fatty or sweet things would precipitate an attack. Previous to this, I was very fond of sweet things, but somehow I seemed to lose my taste for sweetness in food. About ten years ago I lost a favourite brother by drowning and developed rheumatic fever, and was off duty for five months. Prior to this I had had a great deal of worry and overwork. During this period of rheumatic fever, dizziness was less severe and less frequent. I was superannuated on account of my complaint in 1928 and things went along fairly well for that year and the next. I had, however, always to be on my guard as to diet, since very little upset me. Through 1930 I was very ill and I was just recovering at the time of the Hawkes's Bay earthquake of 1931. After that I spent six weeks in camp, and the open care-free life seemed to help me for a time. I relapsed again, and by the end of the year the dizziness and vomiting were getting extreme. The years 1932 and 1933 have been the most consistently ill of all. These dizzy attacks would often wake me during the night and would occur several times during the day. My vision used to become blurred and distorted and I was in a cold profuse perspiration during and after—often, too, prostrate. No special work precipitated an attack, but worry or anxiety made me very prone to them. Talking to two or three people, being in a crowd, concentration, or the sight of revolving motion, would all bring on attacks. For weeks I never felt hungry, but sometimes after a bout of dizziness or when I could not go to sleep, I could have enjoyed a meal, but desisted for fear of bringing on another attack. When vomiting accompanied my attacks, I slept very heavily and was often hungry. My sleep was very profound. After an attack I used to yawn and yawn. The attacks of dizziness certainly affected my memory and intelligence. I could not think as I wished—the effort was too much for me. Exercise did not bring on attacks. During the past year the symptoms have changed. The attacks are now shorter and more severe and have culminated in my being thrown to the ground on several occasions. The first time was a year ago at Christmas, when, about 3 o'clock in the afternoon, I fell flat on my back. I was not giddy and I did not vomit. The next occasion was three weeks later when I was playing the piano. Before I knew what had happened, I had fallen to the floor. On the third occasion I was shopping and I would have fallen if I had not caught hold of an iron standard. The fourth occasion was immediately before my admission to hospital. I did not feel at all well on rising, but after a cup of tea at about 8.30 a.m. I was chatting to some people on the verandah, when all at once I was seized with that awful sensation. I knew what was impending, as this was my fourth ' throw over '. I grabbed the verandah post, hoping to avert a fall, but my arms just had to relax and down I went. I sat up at once and after a short time I recovered a little, and walked into the house without assistance. In the ordinary attacks of dizziness, I had to have assistance in order to move about at all. I then went to bed and did not feel nearly so ill as generally after even a dizzy attack. In fact, I felt pretty well all day."

ON EXAMINATION.—The patient was examined about 10 a.m. on Dec. 8, 1933, soon after her last attack. There was slight nystagmus on looking to the right, the abdominal reflexes were not elicited and the left knee- and left ankle-jerks were much brisker than on the right side. The plantar reflexes were flexor. She was admitted to hospital for investigation and when seen a few hours later these abnormal neurological findings were absent.

Her complexion was sallow. Weight, 7 st. 9¾ lb. Height, 5 ft. 4 in. X-ray of the chest showed "considerable elevation of the diaphragm with increase in left subphrenic opacity. There is very definite mottling of both hilar regions and the right cardiophrenic angle. Heart shadow tilted." X-ray shadows of the gall-bladder showed normal function. X-ray of the skull showed a normal pituitary fossa. A twenty-four-hour specimen of urine (32 oz.) showed 100 units of diastase and was otherwise normal. Blood-count: reds 5,000,000 per c.mm., leucocytes 8,600 per c.mm., Hb 96 per cent, colour index, 0·96. Differential count: polymorphs 57·5 per cent, lymphocytes 30·5 per cent, eosinophils 4·5 per cent, transitionals 5 per cent, basophils 2·5 per cent. Reds appear normal. Van den Bergh: direct reaction negative, indirect very weak positive. Faeces were negative for occult blood; films showed no obvious neutral fat globules and no fatty acid crystals; there was a small amount of soap;

Fig. 39.—Blood-sugar curves with increasing doses of glucose, before operation. –·–·–·–·–·– Average of three curves after ingestion of 50 grm. of glucose. – – After ingestion of 100 grm. – – – – – – – After ingestion of 150 grm. –x–x–x–x–x– After ingestion of 200 grm.

no muscle fibres found. Test-meal showed a normal curve. Blood-pressure: systolic 130 mm. Hg, diastolic 80 mm. Hg. Wassermann and Kahn reactions in blood and cerebrospinal fluid were negative. Neurological and other examinations were normal. There was slight deafness in the right ear, but the tympanic membrane on either side was normal. The thyroid gland was not palpable. The optic discs were normal.

Blood-Sugar Estimations.—A number of blood-sugar estimations were carried out on venous blood by the colorimetric method of Folin and Wu. After the administration of 50 grm. of glucose the curve was always of a hypoglycaemic type, and the average of three such curves before operation is shown in *Fig.* 39. It was decided to carry out tolerance tests with increasing doses of glucose in order to see if any marked difference in the curves resulted. With 100 grm. of glucose the surprising curve shown in *Fig.* 39 was obtained. This curve is referred

to in the discussion.   There was a marked difference between the curves obtained after 150 grm. and after 200 grm. of glucose was given (*Fig.* 39).   A more detailed curve after the administration of 200 grm. of glucose is shown in *Fig.* 40.   The blood-sugar for a fasting day is illustrated in *Fig.* 41.   This shows a gradual rise, with a marked rise in the early afternoon.   *Fig.* 42
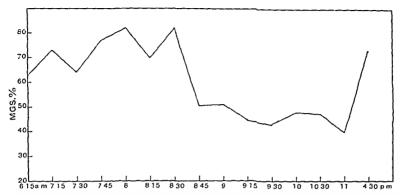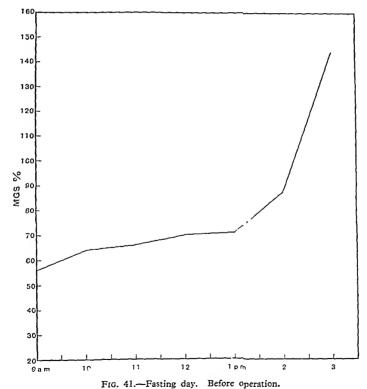

FIG. 40.—Blood-sugar curve after ingestion of 200 grm. of glucose, before operation.   The patient had a meal at midday and later complained of a numbed feeling in the hands.   The glucose was given at 7.15 a.m.

FIG. 41.—Fasting day.   Before operation.

shows the curve obtained after 50 grm. of glucose was given with 50 units of insulin intramuscularly.   Two and a half hours after the test commenced the blood-sugar was 50 mgrm. per cent, and the patient complained of feeling strange.   Three and a half hours after the commencement the capillary blood-sugar was 70 mgrm. per cent, showing that considerable

peripheral storage was therefore taking place at hypoglycæmic levels of blood-sugar, which at the same time was 41 mgrm. per cent   The curve resulting after the administration of 50 grm of glucose with 1 c c. pituitary extract intramuscularly is illustrated in *Fig.* 43   The rise in blood-sugar following a subcutaneous injection of 1 c c. of 1–1000 adrenalin is illustrated in *Fig* 44   The curve obtained after the administration of 50 grm. of glucose with 2 oz of brandy is shown in *Fig.* 45. This curve does not differ materially from those obtained after the administration of 50 grm of glucose alone.
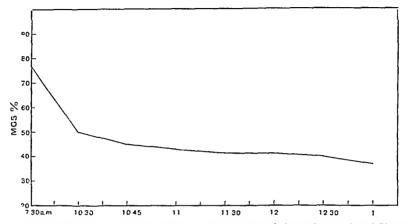
FIG 42 —Blood sugar curve before operation, after 50 grm of glucose by mouth and 50 units of insulin intramuscularly at 8 a m   At 10 30 a m the patient complained of feeling strange. Capillary blood-sugar at 11 30 a m was 70 mgrm per cent
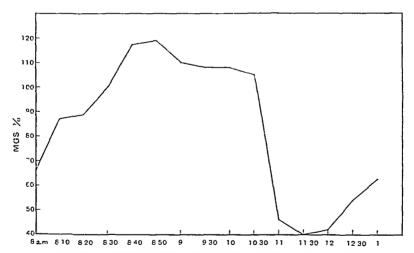

FIG 43 —Blood-sugar curve before operation after 50 grm of glucose by mouth and 1 c c of pituitrin intramuscularly

After a consideration of the various blood-sugar tests the case was thought to be one of hyperinsulinism, and operation was decided upon.

OPERATION (Jan 24, 1934).—I M H. gr. ¼ and hyoscine hydrobromide gr. $\frac{1}{100}$ were given at 7 a m , followed by 5 drachms of paraldehyde with 70 drachms of saline per rectum.   In the operating-theatre 250 c c. of ether was administered.   A left paramedian incision was made with a lateral incision into the flank.   The pancreas and other abdominal organs were examined and found to be normal.   A little more than 28 grm. of pancreas, including the

tail and part of the body, were removed, going through the gastro-hepatic omentum. The operation was technically difficult owing to the fact that the pancreatic veins were exceedingly fragile, tearing out of the splenic vein and needing several lateral ligatures on that vessel. One of the splenic veins during the removal of the tail caused troublesome bleeding. It was
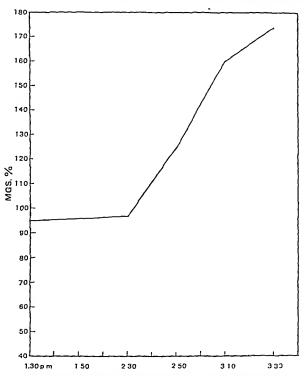

FIG. 44.—Blood-sugar curve before operation after 50 grm. of glucose by mouth and 1 c.c. of 1-1000 adrenalin solution injected subcutaneously at 1.50 p.m. At 3.25 p.m. the capillary blood-sugar was 181 mgrm. per cent.
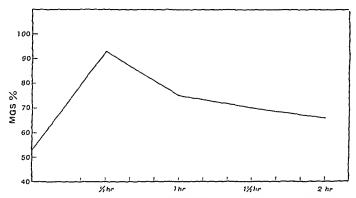
FIG. 45.—Blood-sugar curve before operation after ingestion of 50 grm. of glucose with 2 oz. of brandy.

intended to remove somewhat more of the pancreas, but a large vein passed through the body upwards and towards the left to join the splenic vein. Rubber-covered clamps were applied as close as possible and parallel to this vein, and that portion of the pancreas to the left was removed. The clamps were left in position and removed on the third day.

Following the operation the patient was shocked. At 11.30 a.m. one pint of blood with two pints of saline and gum acacia were given intravenously. At 4 p.m. two pints of 5 per cent glucose with 60 units of insulin were given. At 8 p.m., 6 oz. of urine were passed which contained sugar. On the following morning the patient's condition was satisfactory. The urine contained a large amount of sugar but no acetone bodies. In the evening another blood transfusion of one pint was given. The highest temperature was on the second day following operation, when it reached 102°, and by the fifth day it was normal. There was some serous and later some purulent discharge from the track along which the clamp and forceps had lain, but the wound healed satisfactorily. On Feb. 22 the patient complained of some frequency of micturition. A catheter specimen of urine showed microscopical pus, a number of epithelial cells, and Gram-positive bacilli. This condition persisted for some weeks and bladder irrigations were necessary. The pathological report on the pancreas was : "The structure is that of a normal pancreas. The amount of insulin tissue judged by comparison with a normal pancreas is not more than normal. There is no inflammatory change in the pancreas."
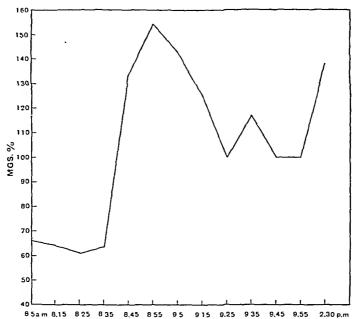

FIG. 46.—Blood-sugar curve during operation. Paraldehyde administered at 8.15 a.m. Ether commenced at 8.45.

Blood-sugar estimations were done at intervals of ten minutes before, during, and after operation (*Fig.* 46). These figures show that the blood-sugar, as is well known, rises during the course of a surgical operation, particularly when ether or chloroform is used.

AFTER-PROGRESS.—While the patient was in hospital she had many attacks of vertigo. Glucose-tolerance tests were carried out during convalescence. Four weeks after operation a diabetic type of curve was obtained after the administration of 50 grm. of glucose (*Fig.* 47). Three months after operation, the curve, after a similar test, had returned almost to what it was before operation (*Fig.* 47). The patient's weight fell from 7 st. 10 lb. to 7 st. 5 lb. a week before operation. When she was next weighed (March 2) she was 6 st. 9 lb. ; on March 17, 7 st. 3 lb. On her discharge from hospital on April 14 her weight was 7 st. 8 lb. Writing recently the patient stated :—

"On June 14 my weight was 9 st. 1 lb. and it has increased to 9 st. 6 lb. at the time of writing, which is my greatest weight for fourteen years. After leaving hospital I had a few touches of dizziness, but these attacks were different from those of the

pre-operative period. They were more transitory in nature—very much less severe—in short, not to be compared with the previous ones. I could, even if slightly dizzy, move about on my own, which was more than was possible previously. I was conscious of a gradual improvement in every way. I can enjoy food and take various articles of diet that I had not cared to touch before, and I have noticed that I want my tea sweeter. I feel every bit as good as I did twenty-five years ago when I enjoyed perfect health. I cannot realize my freedom from that awful affliction."
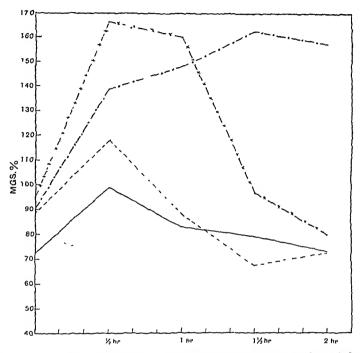
FIG. 47.—Comparison of blood-sugar curves after ingestion of 50 grm. of glucose before and after operation. ———— Before operation. —·—·—·— One month after operation. – – – – – – – Three months after operation. -x-x-x-x- Eight months after operation.

Fig. 47 illustrates in a striking manner the readjustment of carbohydrate metabolism. The hypoglycæmic curve before the operation is shown. Then within four weeks of operation a diabetic type of curve. This was followed three months after operation by a return of the curve almost to its original hypoglycæmic level. Again, eight months after operation the curve is practically normal.

DISCUSSION

Cases of hypoglycæmia may be divided into : (1) Those due to functional hyperinsulinism, whether due to increased number, size, or activity of the islands of Langerhans. (2) Those due to the presence of an adenoma or carcinoma of the pancreas. (3) A medley of cases which come under the heading of 'dysinsulinism.' These are dependent on pituitary, adrenal, hepatic, or other factors.
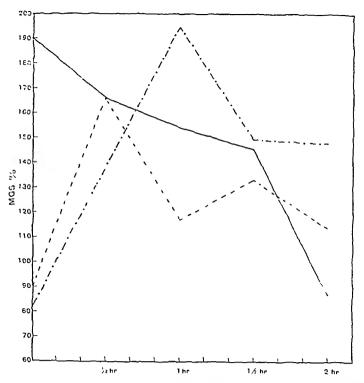
From a perusal of the literature it would appear that the surgical treatment of spontaneous hypoglycæmia, apart from those cases in which an adenoma has been removed, is disappointing. The possibility must be considered that those cases of hyperinsulinism that have not responded to surgical treatment may have

had a small adenoma buried in the head of the pancreas, where it would be difficult or impossible to locate on account of its size.

Best[3] publishes the following table :—

        Cases with no detectable pancreatic lesion
            (Finney, Holman, Allen 2, Mayo 2)   6
        Cases without tumour in which partial pancreatectomy
            was performed   6
        Results of partial pancreatectomy :—
            Reports of improvement unconvincing   1
            No improvement reported   5

With such disappointing results, it is not surprising that John[1] should state : "The operative procedure, with the exception of cases in which there is an adenoma of the pancreas, does not seem a logical solution of the problem of hypoglycæmia."

FIG. 48.—Comparison of blood-sugar curves after ingestion of 100 grm. of glucose before and after operation. ————— Before operation. –·—·—·—·– Five weeks after operation. – – – – – – – Eight months after operation.
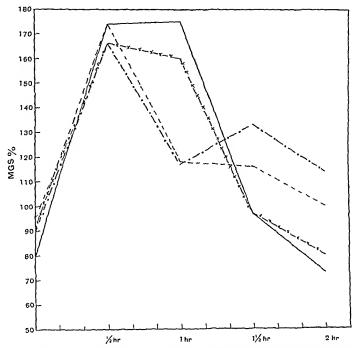
He regards these cases as potentially diabetics, and on this basis treats them by insulin after meals, hoping to avoid hyperglycæmia and to prevent the high blood-sugar stimulating an excess of insulin. By supplying exogenous insulin he attempts to put the pancreas at rest.

Nielsen and Lewis,[5] in a discussion on glucose-tolerance tests in patients with vagotonia, state that these patients experience with peculiar regularity a hypoglycæmic reaction during the course of a glucose-tolerance test. In 21 cases

there were 3 in which the blood-sugar fell immediately after ingestion of 100 grm. of glucose. They concluded that the pancreas was very active, that it was stimulated easily, and acted quickly. In one of their cases the highest point in the course of the test was found in the starvation specimen. In the present case this phenomenon is well illustrated in *Figs.* 39 and 48.

Brougher,[6] in a study of glucose-tolerance tests in 14 patients whom he regarded as hypoglycæmic, noted the frequency with which hypoglycæmic symptoms occurred during the course of the test. In the present case the administration of glucose with insulin was followed by a period in which the patient complained of feeling strange and there was a definite and gradual fall in the blood-sugar (*see Fig.* 42). It would appear that, though the administration of insulin in these

FIG 49 —Blood-sugar curves with increasing doses of glucose eight months after operation
-x-x-\- After ingestion of 50 grm of glucose   -·-·-·- After ingestion of 100 grm   - - - - After ingestion of 150 grm ———— After ingestion of 200 grm

cases may possibly be indicated theoretically, a study of the blood-sugar curve shows that hypoglycæmia is not avoided. It must be noted, however, that Nielsen and Lewis in their conclusions in the paper referred to state : " The hypoglycæmic reaction is not necessarily coincident with hypoglycæmia. There is still some unexplained factor in the production of these reactions. The degree of the reaction bears no direct relation to the depth of the glucose-tolerance curve." It may be possible to associate abnormal curves during a tolerance test with the subjective symptoms of the patient, even though the degree of hypoglycæmia is not necessarily related to the symptoms. The striking blood-sugar curve shown in *Figs.* 39 and 48 after the ingestion of 100 grm. of glucose showed a fasting blood-sugar of 190 mgrm. per cent. This is a very anomalous curve. At 2 a.m. on the day of

the test the patient had a severe attack of vertigo. It was so severe that she said she would certainly have fallen had she been standing. It is possible that the rise in blood-sugar recorded was a compensatory phenomenon, as the test was begun about five hours later at 7 a.m.

Since removal of an adenoma is accompanied by such excellent results, it seems logical that resection of an amount of pancreas equivalent to the hyper-insulinism is the ideal treatment. From the recent blood-sugar curves of the present case (*Fig.* 49), it seems clear that the patient might have been better with a greater removal of pancreatic tissue. Should hypoglycæmia reappear, it would be almost surgically impossible to remove more pancreatic tissue on account of the superior and inferior mesenteric veins passing through the body of the pancreas. Exactly how much pancreas should be removed is a question that will depend on the severity of the symptoms and on the size of the pancreas. In the past resections have certainly been much too small to allow of any permanent improvement. *Table I* shows the amount of pancreas that has been removed in the recorded cases.

RESECTION OF PANCREAS IN HYPERINSULINISM

OBSERVER	AMOUNT OF PANCREAS REMOVED	RESULT
Finney and Finney[7]	22 5 grm.	Slight improvement
Judd[9]	14 grm.	Improvement lasted one year. Later condition worse than before operation
Judd[9]	8 grm.	No improvement
Judd[9]	5 grm.*	No improvement
Holman and Judd[9]	Weight not stated (2 operations)	Slight improvement
Ziskind[10]	7 2 grm.	No improvement
Wormack[11]	" About half " (2 cases)	Improvement
Graham and Hartmann`	80 to 90 per cent	Improvement

* At subsequent operation a piece of pancreas was clamped and allowed to slough away.

Probably half of the pancreas should be removed to obtain satisfactory results. In the classical case recorded by Finney and Finney[7] it is stated that two-thirds of the pancreas was removed, this weighing 22·5 grm. In a footnote the weight of a normal pancreas in a woman is given as 60 grm. It would appear more accurate to describe this resection as one-third of the pancreas unless the organ in their patient was smaller than normal. It would seem that the figures given for dogs—namely, that 80 to 90 per cent of the pancreas has to be removed to cause hyperglycæmia or glycosuria—are much too high for man. There does seem a distinct liability that a patient might be converted into a permanent diabetic by removal of considerably more than half of the pancreas. The diabetic tendency of the present patient lasted only for a short time (*see Fig.* 47). Then there seemed to be an increased activity of the remaining insulin tissues and her condition seemed to have returned almost to her former state (*see Fig.* 47). Since then there has been a change of the blood-sugar curve almost to normal.

In the striking case recorded by Graham and Hartmann,[8] 80 to 90 per cent of pancreatic tissue was removed from a child of 12 months. The blood-sugar, although at first raised to an abnormally high level as a result of removal of so much pancreatic tissue, later became practically normal, and nine months after operation the fasting blood-sugar was 83 mgrm. per 100 c.c. In discussing this case the authors state : " It becomes evident from this brief review of the reported cases that in general the resection of an approximately normal pancreas up to the amount of two-thirds of it (quoting Finney and Finney) is not likely to result in permanent improvement of the chronic hypoglycæmic, except rarely." In view of the doubt as to whether two-thirds of the pancreas was removed in the Finneys' case and of the great improvement in the present case, it would seem that this statement is not in accordance with the facts. On the analogy of thyroid surgery they state : " In line with such reasoning, one might suppose that the failure to obtain permanent and satisfactory results in the majority of cases in which a true tumour has not been found might have been due to the removal of too little pancreatic tissue." In the same article Wormack, of St. Louis, is quoted as having removed half the pancreas in two cases with subsequent alleviation of hypoglycæmic symptoms. Judd,[9] in another paper, states : " The results thus far have not been encouraging, probably because not enough gland has been removed to influence adequate production of insulin. Medical treatment has proved unsatisfactory in cases in which there was a strong tendency to hypoglycæmia." It would seem reasonable to assume that in cases of functional hyperinsulinism the success of surgical treatment of hyperthyroidism will be repeated if sufficient amounts of pancreas are removed, and it is along surgical lines that cure or alleviation of symptoms is to be expected.

If it were possible to distinguish cases of functional hyperinsulinism from those of adenoma of the pancreas, it might be possible before operation to state how much pancreas should be removed. Wilder,[12] in a discussion on hyper-insulinism, states : " The clinical differentiation between cases with and those without tumour has been for us impossible. The severity of the symptoms has been great in both groups of cases. The dextrose-tolerance test has not been helpful."

In reviewing the records concerning cases of spontaneous hypoglycæmia there is no mention of the study of increasing amounts of carbohydrate on the blood-sugar curves. It would seem probable that cases of marked functional hyper-insulinism should react to increasing amounts of carbohydrates by a progressive lowering of the blood-sugar, and that starvation, on the other hand, should allow the blood-sugar to rise. If these postulates should prove true in other cases, then functional hyperinsulinism, whether due to increased number, size, or activity of the islands of Langerhans, should easily be separated from other causes of hypoglycæmia. From a study of the blood-sugar curves in those cases of spontaneous hypoglycæmia due to the presence of an adenoma or carcinoma of the pancreas it is suggested that these tumours are not under nervous or hormonic control and that they are continually secreting insulin. It has also been suggested that there is a secretion from the tumour itself which stimulates insulin secretion.

On examining the numerous blood-sugar curves that were carried out in the present case before operation it was evident that with large doses of glucose the blood-sugar tended to fall, while eight months after operation different doses of

glucose gave almost the same curve (*see Fig.* 49). Doses larger than 200 grm. were not used in any of the tests. On comparing the curves after the administration of 50 and 200 grm. of glucose respectively (*see Figs.* 39 and 50), it will be seen that the curve after the 200-grm. test is continually lower than after the 50-grm. test. The stomach contents were not aspirated and tested for glucose at the end of the tests and it may be argued that there was delayed absorption of glucose owing to the stomach's emptying slowly. As the 200-grm. test was carried out over a period of practically four hours it seems that this argument would not apply. If the pancreas is abnormally sensitive and easily stimulated in functional hyperinsulinism, it seems reasonable to suppose that the greater the amount of glucose
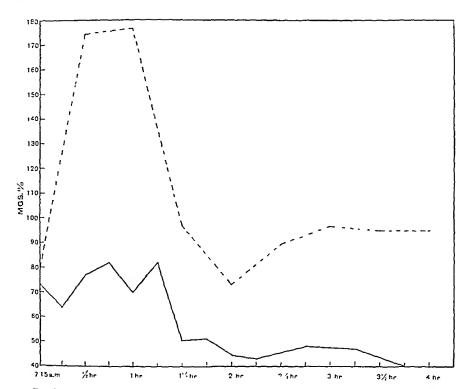

FIG. 50.—Comparison of blood-sugar curves after ingestion of 200 grm. of glucose before and after operation. ———— Before operation. - - - - - After operation.

absorbed into the blood-stream, the greater will be the stimulus to the production of insulin. Hence the decreasing values in the blood-sugar curves with increasing doses of glucose. If it should be proved definitely that the excessive insulin production in a case of adenoma is not dependent on hormonic, nervous, or other control, this test should prove of great value in the differentiation of tumours of the pancreas from functional hyperinsulinism.

It is well known that during starvation the level of the blood-sugar falls very little, and lowering it beyond a certain level cannot be effected by complete deprivation of food, however prolonged. In this case starvation actually resulted in a rise in blood-sugar (*see Fig.* 41). It is difficult to understand why this should occur.

Possibly there was a lack of stimulus to the pancreas during the period of starvation and consequently insulin production was diminished, allowing the blood-sugar to rise. It would have been expected that when the blood-sugar had reached a certain value, more insulin would have been produced, causing a hypoglycæmic reaction. It is suggested that this rise in blood-sugar during starvation may be confined to cases of functional hyperinsulinism and may prove a ready means of distinguishing this condition from a tumour of the pancreas. It is hoped that, by drawing attention to this phenomenon and to the probability that large doses
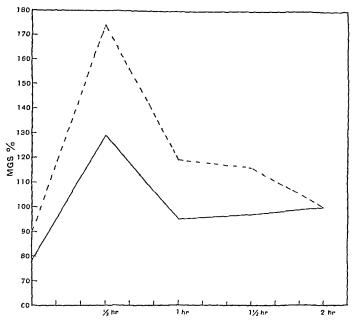
Fig. 51.—Comparison of blood-sugar curves after ingestion of 150 grm. of glucose before and after operation   ————— Before operation.   – – – – – After operation.

of glucose in cases of functional hyperinsulinism lower the blood-sugar, these tests will be carried out in future cases of spontaneous hypoglycæmia in which surgical intervention is contemplated. Only by this means can the value of these tests be proved.

SUMMARY AND CONCLUSIONS

1. A case of hyperinsulinism is described.
2. Partial pancreatectomy was performed, 28 grm. of pancreas being removed.
3. Glucose-tolerance tests performed before and after operation are discussed.
4. The following hypotheses are put forward: (a) Adequate resection, probably more than half of the pancreas, in a moderately severe case of functional hyperinsulinism is necessary to alleviate symptoms. (b) In the diagnosis of functional hyperinsulinism increasing doses of glucose are necessary in preparing blood-sugar curves, and the curves are lower with the large doses. (c) In functional hyperinsulinism starvation causes a rise in blood-sugar.

5. It is suggested that these two tests may be of value in distinguishing functional hyperinsulinism from an adenoma or carcinoma of the pancreas.

I wish to thank Messrs. S. W. Saunders and G. W. McKinley for performing the numerous blood-sugar estimations in this case.

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CONGENITAL DERMOID CYSTS AND SINUSES OF THE LIMBS

By M. J. BENNETT-JONES

SURGICAL REGISTRAR, LIVERPOOL ROYAL INFIRMARY

CONGENITAL dermoid cysts and sinuses associated with the limbs appear to be very rare and to have escaped description in the English surgical literature. Dieterich, however, records a dermoid cyst of the shoulder, and Phélip has described a congenital dermoid cyst occurring on the index finger of an infant aged 13 months. Epiphanov has also described a cystic dermoid femoral hernia. Apart from these cases, Paterson, Cisneros, and others have described dermoid cysts occurring in
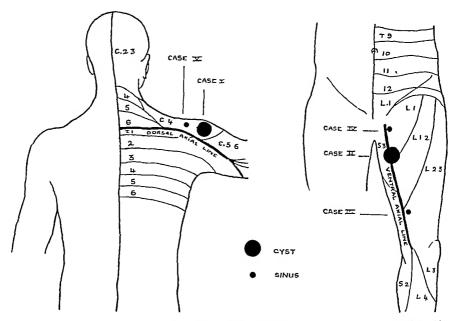
FIG. 52.—Diagram showing dorsal and ventral axial lines and the sites of the congenital dermoid cysts and sinuses recorded.

the inguinal canal, and Bland-Sutton has recorded the removal of a very large dermoid cyst of the right labium majus ; these latter cases, however, did not occur on the limbs, although they probably had the same etiology.

Etiology.—The limbs arise as buds from the ventro-lateral aspect of the trunk and they are composed of a number of body segments. Owing to the fact that the more peripheral part of the limbs is derived from the middle segments of the limb bud, there is formed a dorsal and ventral axial line in the proximal portions of the limbs, between the upper and lower segmental portions. These

axial lines appear to be the most common site for dermoid cysts and sinuses associated with the limbs (*Fig.* 52).

Clinical Features.—In the appended short series of cases a dermoid cyst and dermoid sinus were seen near the tip of the shoulder. This position marks the boundary between the areas of skin supplied by the cervical and brachial plexuses; this position is also very near, if not coincident with, the dorsal axial line of the upper limb.

In the lower limb three cases were seen. A dermoid sinus was observed between the posterior end of the labium majus and the thigh. A dermoid cyst was removed from the inner side of the upper third of the thigh, and a dermoid sinus was seen on the inner aspect of the lower third of the thigh. It is interesting to note that these three cases occurred on the ventral axial line of the lower limb.

Two cases were associated with other congenital deformities. The sinus between the thigh and the labium majus was associated with a recto-vaginal fistula and spina bifida occulta; and the sinus in the lower third of the thigh was associated with an accessory hallux.

Conclusion.—Although both the dermoid cysts were diagnosed as lipomata, these cases have no great surgical importance. This series, supported by Phélip's case, does, however, raise the possibility that some, at least, of the so-called traumatic epithelial cysts of the hand may be congenital in origin. These cases, however, have an embryological significance and they help to confirm Sherrington's work on the segmental nerve-supply of the limbs which was worked out experimentally on apes.

CASE REPORTS

Case 1.—Male, aged 23. Admitted into the Liverpool Royal Infirmary.

HISTORY.—A swelling on the right shoulder was noticed soon after birth. It enlarged very slowly, but lately became tender and the overlying skin became red, so that the patient desired removal of the swelling.

ON EXAMINATION.—Very soft, fluctuant, non-translucent swelling situated in the subcutaneous tissue superficial to the acromion process near its tip. The swelling was about $1\frac{1}{2}$ in. in diameter and was not lobulated. The adherent overlying skin was tense and red.

OPERATION (Mr. Nuttall, Dec. 9, 1933).—The tumour was found to be a dermoid cyst and was, therefore, easily excised.

PATHOLOGICAL REPORT (Dr. T. B. Davie).—The cyst is lined by typical squamous epithelium of a dermoid.

Case 2.—Female, aged 32. Admitted into the Liverpool Royal Infirmary.

HISTORY.—A lump appeared on the inner side of the left thigh at least ten years ago. It enlarged very slowly, but at times it became painful and slightly tender. After the operation the patient was questioned about any possible injury or puncture of the thigh, but neither could be remembered. Lately another lump appeared in the right groin which caused the patient to seek advice.

ON EXAMINATION.—Spherical, non-translucent, fluctuant swelling about $1\frac{1}{2}$ in. in diameter situated on the inner aspect of the upper third of the left thigh. No attachment to the overlying skin or the underlying adductor magnus muscle. No impulse on coughing. The lump in the right groin was a typical femoral hernia.

OPERATION (Mr. Nuttall, Oct. 12, 1933).—Repair of right femoral hernia by Lotheissen's method. Excision of a cyst of the left thigh, which was found to be a typical dermoid cyst.

PATHOLOGICAL REPORT (Professor Dible).—Squamous epithelial cyst.

Case 3.—Male, aged 2. Admitted into the Hospital for Sick Children, Great Ormond Street.

HISTORY.—The child's mother brought him to hospital because an accessory toe prevented

his obtaining shoes which fitted. The child also had a sinus on the inner side of the left thigh which had been present since birth. Occasionally a swelling appeared deep to the sinus, but it soon disappeared by discharging through the sinus.

ON EXAMINATION.—Small epithelial sinus on the inner aspect of the lower third of the left thigh, superficial to the internal intermuscular septum. No swelling deep to the sinus at present, but a swelling was seen in the Out-patient Department. An accessory left hallux was present.

SUBSEQUENT HISTORY.—

Oct. 29, 1932.—Mr. Tyrrell-Gray amputated the 2nd toe including its metatarsal after consultation with Mr. Fairbank, but no operation was performed on the sinus.

Jan. 5, 1935.—The mother states that the sinus is giving no trouble at present, although it occasionally discharges.

Case 4.—Female, aged 8 months. Under the care of Mr. W. A. Thompson at the Royal Liverpool Children's Hospital.

HISTORY.—The child was brought to hospital on account of a recto-vaginal fistula. The mother also noticed a sinus near the right labium majus which occasionally discharged.

ON EXAMINATION.—A recto-vaginal fistula was present associated with an imperforate anus and spina bifida occulta. Epithelial sinus situated between the posterior end of the right labium majus and the right thigh. No discharge at present.

Case 5.—Female, aged about 50. A patient of Mr. Grant Massie at Guy's Hospital.

HISTORY.—For many years she had a sinus near the tip of the right shoulder which discharged intermittently.

ON EXAMINATION.—Sinus near the tip of the right shoulder, with the typical foul smell of decomposing dermoid secretions.

SUBSEQUENT HISTORY.—She became frightened after a demonstration and she did not turn up again, and could not be traced.

This case, therefore, is not confirmed by operation and there was no proof that the sinus was congenital, but at the time it was thought to be a dermoid sinus, and, moreover, it occurred in the same situation as the dermoid cyst on the shoulder (*Case* 1).

I wish to thank the surgeons of the various hospitals for permission to record their cases.

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ACROMEGALY

By R. LAWFORD KNAGGS, Newton Abbot

" ACROMEGALY is a chronic disease of adult life outwardly characterized by the acral changes first emphasized by Marie ", and believed to be dependent on a hyperplasia of certain granular cells in the anterior lobe of the pituitary body, which in many instances produces an enlargement or a tumour (Cushing and Davidoff).

A Synopsis of the Pituitary Disorders.—The growth disorders known as acromegaly, giantism, and infantilism constitute a group of affections which are believed to depend largely upon abnormalities of pituitary gland secretion. Besides having a common glandular origin they are further correlated. Giantism tends to merge into acromegaly, and acromegaly, after persisting for a number of years, acquires some of the features of infantilism.

There is no doubt that giantism and acromegaly result from excessive secretion of the anterior lobe, usually as a consequence of hyperplasia of its cells, though in rare instances it may possibly be due to their physiological over-activity; on the other hand, the supervention of some of the signs of infantilism is supposed to mark the waning of the hypersecretion and the access of a state of deficient secretion (hyposecretion) resulting from the inaction or exhaustion of the anterior lobe.

The following scheme of the conditions dependent upon abnormalities of the pituitary secretion has been compiled from Harvey Cushing's *Pituitary Body and its Disorders* (1912), a book so full of clinical and experimental facts that in the future much valuable information will be quarried from it.

Cushing recognized three symptom-groups determined by variations of the pituitary secretion : (1) Hyperpituitarism, in which the anterior lobe secretion is increased (over-activity); (2) Hypopituitarism, in which the anterior lobe secretion fails or is insufficient (under-activity); and (3) Dyspituitarism, in which the symptom-groups are mixed, and it may be difficult to tell whether the hyper- or the hypopituitary state predominates. These are transition cases, and constitute the majority.

1. *Hyperpituitarism.*—From hyperpituitarism result :—
    a. Giantism, when the process occurs before the epiphyses have united with the shafts of the long bones (Type of Launois).
    b. Acromegaly, when it occurs later—in adult life (Type of Marie).
2. *Hypopituitarism.*—
    a. When the disorder originates in childhood there is adiposity with skeletal and sexual infantilism (Type of Fröhlich).
    b. In some cases adiposity is absent—"an adult in a small mould" (Type of Lorain).
    c. When the affection begins in adult life it produces adiposity and sexual infantilism of a reversionary type; i.e., sexual adolescence occurs before the symptoms of hypopituitarism develop (Type of Harvey Cushing).

3. *Dyspituitarism.*—In dyspituitarism the signs of pituitary under-activity constitute the striking feature, but manifestations of a previous hyperpituitarism in the shape of acromegalic changes are present.

4. Cushing included under dyspituitary states two case-groups. His fourth group—in which secondary disturbance of the pituitary is produced by remote, rather than local, intracranial lesions; and

5. His fifth group, in which the signs and symptoms point to involvement of several of the ductless glands—the *pluri- or polyglandular affection.* It is the latter group with which acromegaly is sometimes associated.

INTRODUCTION

The year 1886 is a landmark in the story of acromegaly. Before that date certain peculiar appearances, seen in rare and occasional cases, had attracted attention, but they were not understood, even when Pierre Marie,[1] in a celebrated paper, described the condition and showed that it was identical with that depicted in a number of recorded cases. As a result of his observations Marie concluded that " there exists an affection characterized chiefly by hypertrophy of the feet, hands, and face, which I propose to call ' acromegaly ', that is to say, hypertrophy of the extremities "; " not," he added, " that in reality the extremities only are attacked during the duration of the malady, but because their increase in size is an initial phenomenon, and constitutes the most characteristic feature of the affection."

A descriptive record of these early cases is readily accessible in the monographs of Sternberg and Souza-Leite* translated respectively by F. W. Atkinson and P. S. Hutchinson,[2] but a few of the more notable ones are referred to below to give a general impression of the disease as it was understood after the publication of Marie's article.

Case 1.—The first case in England of which there is any note was a certain Richard Dickenson (*Fig.* 53), a shoe-cleaner and vendor of gingerbread, who subsequently became ' Governor of Scarborough Spaw (Spa) and lavatory attendant ' He was, in his way, a celebrity, and well known to visitors. He died in 1738 at the age of 68. Five different portraits of him are extant, and three were reproduced in an interesting account by L. P. Mark.[3] They show the characteristic signs of acromegaly and, in addition, deformities which were probably due to rickets.

Case 2.—Henrot gave to this case the name of "general progressive hypertrophy" (1877), and it is of special importance because a pituitary tumour was present. The particulars are as follows : Alphonse D— was 38 years old when he died. From the age of 6 he had general increasing swellings of the submaxillary cervical glands, which never suppurated, and eventually filled the whole front of the neck and overlapped the lower jaw. The blood showed no leucocythæmia. He noticed progressive enlargement of the hands and feet from the age of 15, was in a dragoon regiment at 20, and for the last five years of his life worked in the cellars (Rheims). His face was repulsive, his appetite large, and his thirst abnormal. For the rest, it is sufficient to quote the abstract which prefaces the account :[1] " Cervical adenia ; slight

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* The earliest known suggestion of acromegaly occurs in a sculptured figure on Rheims Cathedral (thirteenth century). *Art frequently makes use of diseased conditions to represent the grotesque,* and a quite recently much discussed statue called ' Genesis ' exhibits the characteristic features of the disease. It goes astray, however, in one point. The obese stage of the affection, which the figure portrays, is incompatible with either conception or pregnancy.

diabetes; hypertrophy of hands, feet, lower jaw, and tongue; exophthalmos, impaired vision; hypertrophy of the pituitary body, of the pineal gland, of the great sympathetic, of the liver, spleen, and kidneys; atrophy of the heart and arteries." The pituitary tumour was the size of a small hen's egg, had enlarged the fossa, flattened the chiasma, and excavated the sphenoidal lobes.

Case 3.—This was recorded by Cunningham[5] (1879) and named, after Henrot's, "general progressive hypertrophy". Subsequently to Marie's paper, Alexis Thomson[6] described the skeleton and pronounced it to be acromegalic. It was that of a dissecting-room subject who had been in the Royal Infirmary, Edinburgh, for diabetes and who was thus described by his physician, Dr. Muirhead : " The whole aspect and general configuration was so peculiar as at once to arrest the attention of an observant person. His frame was so huge, his movements so ungainly, his expression so unpleasing, his brow so overhanging, and the hands and feet so enormously enlarged as to suggest the idea to some in the ward of a resemblance to a gorilla, and by this epithet he was known amongst the other patients." He was 6 ft. ¼ in. high, the circumference of his head was 24¼ in., his chest measured 43 in. at the nipple line, and 46 in. three inches below. The pituitary body was as large as a walnut, projected upwards from the expanded fossa, and had hollowed out the base of the brain for its reception.*

Case 4.—This was shown by Haddon and Ballance[7] in 1885 as "hypertrophy of the subcutaneous tissue of the face, hands and feet", and published in 1888 as an example of the disease described by Marie. The patient, a woman aged 37, dated her disease to an attack of scarlet fever contracted from her children, and followed by rheumatic swelling of both knees. Her hands began to swell shortly after. The catamenia had ceased permanently a few months before, and a photograph taken just before the scarlet fever showed that her appearance had undergone a striking change. She was a big-featured woman, with broad lower jaw, and thick everted lower lip. The uniform

FIG. 53.—Richard Dickenson, who died in 1738, aged 68. Probably the earliest case of acromegaly in England of which there is any note. (*From a small picture in the R.C.S. Museum.*)

enlargement of both jaws was, apparently, simple hypertrophy. The nasal enlargement was due to hypertrophy of the nasal cartilages and the overlying tissues, the nasal bones being unaffected. The clavicles were larger and thicker than normal and much curved; the hands and feet were gigantic but not deformed, and the subcutaneous fatty tissue was probably disproportionately thickened. In contrast with the hands and feet, the forearms and legs were not enlarged. The speech was guttural and the tongue large, and the right optic disc was atrophied.

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* The following observation by Sir Arthur Keith may be quoted here. " I do not for a moment suggest that the Neanderthal race suffered from acromegaly nor that acromegaly is a resurrection of the anthropoid state. From what is known of the function of the pituitary it may be stated with some degree of assurance that all three—the gorilla, the Neanderthal man, and the acromegalic—suffer from that condition known as hyperpituitarism " (*Lancet*, 1911, April 15, 993).

A pituitary tumour had been noted in several of the cases which later on came to be identified with acromegaly, and intracranial changes pointing to pituitary tumour were subsequently found in Marie's second case (Broca[8]), but the importance of this combination was not fully appreciated, the enlargement being looked upon as part of the general hypertrophy.   But the constant association of pituitary tumour became steadily more certain, and in in 1898 Furnivall[9] showed that in 49 post-mortems on acromegalic cases the pituitary was affected in all, and was enlarged or the seat of tumour in all but two or three.   (*Fig. 54.*)

With the discovery of the X rays it soon became possible to recognize an increase in the size of the pituitary fossa during life, and even to trace advancing deformation as the pituitary disease slowly advanced.   When it once became clear
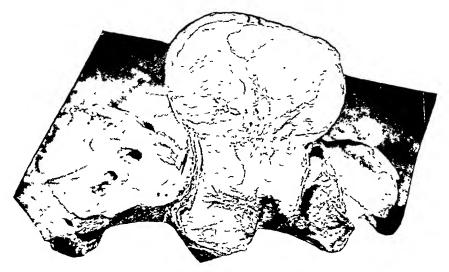
FIG 54 —A pituitary tumour in a case of acromegaly.   Messrs. Neal and Shattock's case.   A woman, aged 41, in whom the disease had existed for eighteen years, was admitted to Wandsworth Infirmary with well-marked acromegaly, general muscular wasting, loss of power, and very dull mental state. Death from pneumonia   "Histologically the tissue closely resembles that of the anterior glandular lobe of the normal organ."   (*Trans. Pathol. Soc*, 1898, xlix, 224)   (*R.C.S. Museum No.* 48.1.)

than an enlargement of the pituitary body was definitely associated with Marie's syndrome—by which term hypertrophy of the acral parts is generally understood*— attention was naturally focused upon the gland and its functions.

Numerous investigations, both experimental and clinical, have resulted in the accumulation of a great quantity of information, and as knowledge has increased, interest has spread from the pituitary body and infundibulum to that portion of the base of the brain which lies behind the optic chiasma and in front of the cerebral peduncles.   This forms the floor of the third ventricle and is often referred to by the somewhat indefinite term 'hypothalamus'.

Giantism.—After Marie's recognition of acromegaly as a distinct affection it was quickly pointed out that similar hypertrophy of the terminal parts occurred in many giants.   The preserved skeletons of certain well-known giants were found

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* In Cushing's opinion acromegaly should not be diagnosed in the absence of Marie's syndrome.

not only to exhibit enlarged hands, feet, and jaws, but to have enlarged or deformed pituitary fossæ (*Figs.* 55, 56). The connection between giantism and acromegaly could not be doubted, and it was evident that the increase of stature characteristic
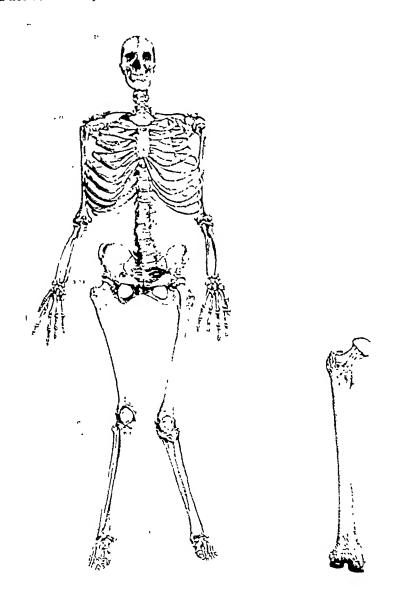
FIG. 55.—The skeleton of Cornelius Magrath, an acromegalic giant. His height was 7 ft. 1⅝ in. His hands were as large as a middling shoulder of mutton, and his shoe last measured 15 in. He was born in 1736 and died in 1775, probably from phthisis. The skeleton is in the Museum of Anatomy and Zoology, Anthropological Section, Trinity College, Dublin. (Cunningham, *Trans. Roy. Irish Acad.*, 1887–92, xxix, 553.)

of the former condition took place in adolescence before the epiphyses became united to the shafts of the long bones. Though acromegalics form a considerable

proportion of all giants, not every giant develops acromegalic characters : 34 recorded giants were enumerated by Sternberg, but only 14 were acromegalics.
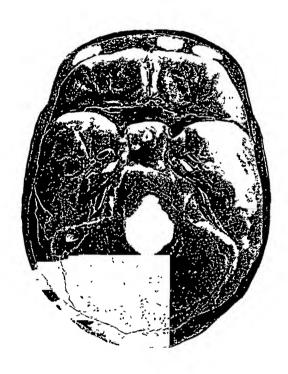
FIG. 56.—The base of Magrath's skull. Note the enlargement of the pituitary fossa, the extent of the frontal sinuses, the hypertrophy of the bones, and the shape of the foramen magnum.

THE CLINICAL FEATURES

The clinical perplexities of acromegaly may be simplified by remembering that : (1) Some of the signs and symptoms depend upon excessive secretion of the anterior lobe of the pituitary; (2) Others may be of local origin, and caused by the pressure of the enlarged pituitary body; (3) It is still undecided whether certain symptoms are of pituitary or cerebral causation; and (4) A few seem to have some relation to other endocrine glands, such as the testicle, the thyroid, the adrenal, and possibly the pancreas. This association may be due to interaction of the duct-less glands, or to their activation by the same stimulus that excites the pituitary.

The onset of the disorder usually occurs in the third or fourth decade. It is more common in the third, but it is infrequent in adolescence and particularly so in childhood.* The affection is usually very chronic, and many sufferers live to

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* When hyperpituitarism occurs in the very young, it does not necessarily lead to giantism. The explanation is supposed to lie in early union of the epiphyses, and without this all cases of acromegaly stated to have occurred in childhood are, in Cushing's opinion, contestable. F. R. B. Atkinson has collected 32 cases from literature, which occurred between the ages of 6 and 14 years. Of these he rejects 8 as doubtful, and, of the remaining 24, giantism was combined with acromegaly in 6. (*Brit. Jour. Child. Dis.*, 1931, xxviii, 121.)

a good age. Three types have been defined (Sternberg) : (1) A benign form which may last as long as 50 years ; (2) The ordinary chronic type with a duration of 8 to 30 years ; (3) An acute form, which may run its course in 3 or 4 years. Cases in the last group are usually malignant, and only nine were known to have occurred when H. D. Rolleston[10] recorded the following instance :—

Case 5.—A woman aged 35 years was a well-marked case of acromegaly. "Enlargement of the hands dated from the early part of 1894, though the patient had not been well since the birth of a child in 1891. The characteristic skeletal changes were present in addition to advanced double optic atrophy and transient glycosuria." "Death took place in coma on Aug. 16, 1897, after an epileptiform fit, of which she had had several since June, 1897." The post-mortem revealed a soft creamy pituitary tumour, a round-celled sarcoma, which had invaded the base of the brain, the right cavernous sinus, the tip of the petrous bone, damaged both optic tracts, and deeply excavated the sella turcica. From the length of the history the growth may have been a malignant termination of an adenoma—of which, however, there was no evidence.

The distinguishing signs of acromegaly are the great enlargement of the hands and feet, and the remarkable alteration of the face. These changes are so characteristic that acromegalics may often be recognized in the streets ; but their onset is so insidious that the sufferer may be unaware of them until his attention is attracted by the increasing size of his gloves, boots, and hat. L. P. Mark,[11] who described his own case, believed his first symptoms occurred when he was 24, but he was 50 before he realized, quite suddenly, that he was an acromegalic, though some of his medical friends had known it for a good many years.

The period antecedent to the development of Marie's syndrome is sometimes comparatively free from symptoms ; on the other hand, it may be a time of great distress owing to various subjective discomforts.* In this prodromal stage two

* Dr. Mark's account of his sufferings is interesting. He writes of ' queer feelings ' which tended to become more constant and to occur at different times of the day ; of an inability to resist cold and exposure, and a liability to cold in the head with abundant rhinorrhœa ; of depression of spirits, asthenopia, and an overpowering desire to sleep, to which he would succumb even when sitting upright.

He describes the condition into which he would frequently lapse when this ' *acromegalic state* ' came on. The ' state ' might be merely an uncomfortable feeling or malaise, but in the severe form he would feel very ill, and for a while quite incapacitated. It might last only half an hour or, on his bad days, from morning to night with slight intermissions—probably just after a meal or sleep. When in the ' state ' his face became pale, the eyes more sunken, the lids puffy and red, and the lower lip more prominent and drooping. Tears would flow so abundantly that he had to mop his face every few minutes. His hands and feet would perspire and become cold, and he had to change his socks. The acromegalic facies became more decided. The ' state ' seemed intimately associated with headache and face-ache. It was not due to fatigue, for it was always worst in the morning. Finally he became depressed by his helplessness and the need to avoid mental or physical effort, and though he could pull himself together by an effort, a corresponding collapse would follow.

For twenty-five years (at the time of writing, 1912[11]) his existence had been a continual fight against this ' state '. It had forced him to regulate his actions to avoid its occurrence at the wrong moment, and it had influenced his life history and his whole mode of life. It reached its climax when he was 38, during a week that he called ' his black week ' in which the neuralgia, asthenopia, and nasal catarrh were worse than they had ever been. From that week the intensity of his troubles gradually declined. Fifteen years later, when he had been an acromegalic forty-eight years, he gave an account of the later phases of his case (" Apologia of an Acromegalic", *Med. Press and Circular*, 1927, Oct. 5 and 12). Apparently the disease had stopped. There had been no increase in size in the jaw, the hands, or the feet for ten or twelve years. He had worn his last denture for twenty years, though previously frequent alteration had been necessary to enable his teeth to meet. His heart, eyes, and his headaches were much less troublesome than formerly, but a state of discomfort " which he could only connect locally with the left side of his head occurred now and then."

He adds a note that the subject of Cushing's Case XXV wrote that his case was strikingly parallel to Mark's. Dr. Mark died in 1930 and bequeathed his body to St. Bartholomew's Hospital for scientific investigation.

grave symptoms may make their appearance, viz., *bitemporal headache and impairment of vision.* The former is caused by the pressure of the enlarging gland upon its fibrous envelope, and is relieved when this is split in an operation, or if spontaneous decompression with expansion into the sphenoidal cells takes place. On the other hand, the bitemporal character of the pain is changed to that suggestive of general intracranial pressure if the tumour bursts through the upper coverings and projects into the cranial cavity.

Failure of sight is usually due to primary optic atrophy, which results from pressure of the tumour upon the optic tracts, the chiasma, or the optic nerves. Bitemporal or homonymous hemianopsia is present at some time in many cases, but there is no rule, and one eye may be blind, and the visual field in the other only slightly affected. A choked disc may be grafted upon the atrophy, if the tumour growth has caused a rise of general intracranial pressure. The latter probably depends upon closure of the foramina of Monro and dilatation of the lateral ventricles, and may be associated with an abrupt onset of " increased headache and possibly vomiting ".

As the chiasma and tracts are pressed upon only when the pituitary tumour expands upwards, many acromegalics are spared visual disturbance. On the other hand, in cases of primary hypopituitarism marked by infantilism and adiposity in which acromegaly is not present, the optic apparatus frequently suffers seriously.

The diagnostic signs of Marie present the following characters. The enlargement of the *hands and feet* is symmetrical and may be enormous, but those parts are not otherwise deformed. The hypertrophy does not extend above the wrist and ankles, and the forearms and legs are normal. It is easy to realize, even without a radiogram, that the increased size and thickness is only in part due to the bones, and that the skin and subcutaneous tissues take an important share in it. The skin is thick and coarse, and the furrows are deep ; the subcutaneous thickening may involve the muscles and by extending between the metacarpal bones may separate them and cause the fingers to diverge.*

Two forms of enlarged hands were described by Marie,[12] the type ' en large ', or shoulder-of-mutton hand, when the onset of acromegaly is late (i.e., in adults), and the type ' en long ', when it is early. In the latter there is considerable increase in length of the metacarpal bones and phalanges.

Remarkable changes occur in the face. It may assume an elongated oval shape (*see Fig.* 63) due to lengthening of the mandible and the sloping of the forehead caused by expansion of the frontal sinuses ; or a square form from hypertrophy of the jaws, malar bones, and zygomatic arches. The orbital ridges, the cheekbones, and the mandible are very prominent, and the overgrowth of the jaws is responsible for a high palate arch, a widening of the mandibular arch, a projection of the chin, and a misfit of the teeth.†

Owing to the prominence of the orbital ridges the *eyes* are apt to be deeply seated, but in some instances they are so prominent that exophthalmos may be

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* Cases have been reported in which rapid and remarkable diminution of the large extremities has followed extirpation of the pituitary tumour ; so rapid may the disappearance be that it is almost certain that some of the enlargement is due to œdema (Cushing's Case XXVI, and Hochenegg's case, *Wien. klin. Woch.*, 1909, 323).

† Mark attributed his indigestion to this misfit, and was greatly relieved by changes in a specially contrived denture from time to time.

said to be present. The latter may be due to hypertrophy of the orbital walls or to changes in the soft tissues of the orbit consequent upon the presence of the intracranial tumour (*see also* p. 81).

The *tongue* is sometimes enlarged to such a degree that it may protrude between the teeth and cause difficulty in speaking, whilst the voice is apt to be harsh and guttural, because the larynx is increased in size and its lining membrane thickened.

The *nose* is large and broad and the skin covering it coarse and thick. The *eyelids* and *lips* are swollen and the lower lip is prominent and everted (*see Fig.* 63).

In addition to Marie's syndrome the increase of the clavicles in length and thickness imparts an unusual breadth to a *chest* which is often enormously enlarged, flattened at the sides, and very deep in the antero-posterior diameter, especially at the lower part. The *spine* commonly presents a cervico-dorsal kyphotic curve, and this may be combined with a lordosis which is probably compensatory.

The examination of the *skull* by the X rays will usually demonstrate some thickening of the cranial vault and considerable enlargement of the air sinuses, especially the frontal and maxillary. As a rule there is more or less alteration of the pituitary fossa, and possibly of its relation to the sphenoidal sinuses. On the other hand, a normal sella turcica may be present when acromegalic signs are marked. A greatly enlarged fossa may be expected when the local signs of tumour are pronounced, but even when they are absent it may be large (*Fig.* 57).

FIG. 57.—Skiagram of the skull of a case of well-marked acromegaly, showing hypertrophy of the cranial vault, enlarged frontal sinus, great enlargement of the pituitary fossa, and prognathous and elongated mandible (*see Fig.* 58). (*Lambeth Hospital records—through the courtesy of Drs. Baly and Stebbing*)

If allowance is made for the slight magnification that occurs on an X-ray plate, the size of the sella may be gauged from a radiogram; "profile measurements", according to Cushing, "exceeding 15 mm. antero-posteriorly and 10 mm. in depth may be looked upon as indicating enlargement".

The same surgeon has described three different forms of sellar enlargement met with in pituitary affections.

1. The first is confined to cases of acromegaly and giantism *without* adenomatous struma formation. In this form the sellar walls are thickened—an expression probably of the general tendency to bony overgrowth.

2. The second may occur in acromegaly, but is rare unless the hypertrophied gland has become an adenomatous struma. In this variety there is marked thinning and perforation of the floor of the fossa, which may be ballooned and project far into the sphenoidal cells, "the bony capsule being so thin as to cast hardly a perceptible shadow". The changes suggest an advanced stage of the affection when the signs of hyperpituitarism have probably been succeeded by those of hypopituitarism.

3. The third shows "more or less complete absorption of the dorsum, and a downward dislocation of the base, so that the sellar landmarks, with the usual exception of the anterior clinoid processes, are effaced". This form may point to primary glandular tumour which has become malignant and burst its dural capsule, or to an interpeduncular tumour which has eroded the subjacent sphenoid.

The changes in the fossa revealed by the X rays are important not only from a diagnostic point of view, but because they may help the surgeon to infer active tumour growth if successive films show increasing destruction.

The So-called Hypopituitary Syndrome.—Sooner or later in the course of the disease certain significant symptoms develop to which the term 'hypopituitary syndrome' has been given. They are: (1) Failure of strength, etc.; (2) A tendency for the patient to put on fat; (3) A high degree of sugar tolerance; (4) The loss of sexual desire and power; and in some cases a transient or permanent polyuria (diabetes insipidus). Some of these symptoms deserve a fuller consideration.*

Adiposity.—There is a tendency to the eventual deposition of fat in all acromegalics and giants, just as there is in eunuchs and in myxœdema; but the

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* Sainton and State (*Rev. neurol.*, 1900, viii, 302) have pointed out that in some cases of acromegaly there is a good deal of pain ("la forme douloureux d'acromegalie"), and they have arranged the various forms of pain that occur into the following groups: (1) Osteo-articular pains, many of which are apparently associated with the increase of growth; (2) Neuralgic pains; (3) Muscular pains—cramps; (4) Pains resembling tabetic crises; (5) Extremity pains—acroparæsthesia. These groups fall into two classes: (1) The rheumatoid type forms which constitute the pains of onset; and (2) Those that depend upon some alteration in the peripheral or central nervous system, 'the hyperalgique type'. The latter are *signs of the cachectic period of the malady*. In a case in which muscular cramps were a prominent symptom they found osseous plaques in the D.M. (spinal) with calcareous granules on its inner surface and a cord lesion chiefly affecting the columns of Goll. They attributed the pains to mechanical pressure of the nerve-roots by the calcareous plates.

Sternberg (*Ibid.*, p. 37) refers to several cases (Henrot's, Duchesnan's, Linsmayer's) in which the arachnoid contained either strongly marked or many small plates of chalk. A somewhat similar condition is described by J. H. Sheldon in an unusual case associated with acromegalic giantism (*Brit. Jour. Surg.*, 1929, xvi, 405). Though Sternberg did not consider this condition as having any pathological significance, yet in the light of the researches of Leriche and Policard (*Les Problèmes de la Physiologie normale et pathologique des Os*) on the nature of ossification it is quite probable that in acromegaly it is associated with the excessive bone absorption of the later stages, and therefore it may be directly connected with the affection.

hypophysial type of adiposity is the common one (Cushing). Possibly in all three it is connected with deficient secretion of the ductless gland specially concerned, i.e., the pituitary in acromegalics, the testes in eunuchs, and the thyroid in the myxœdematous. The fat in acromegalic cases is evenly distributed (*Fig.* 58), but is not limited to the subcutaneous tissue. Fatty masses may form about the viscera, and their substance even may be invaded; in the liver especially there is often extensive replacement of the cells by fat globules.

The accumulation of fat is usually associated with an ability to assimilate excessive amounts of sugar, but the quantity reaching the blood is markedly subnormal (hypoglycæmia). It is practically certain that most of the sugar is converted into fat, and that sugar metabolism is largely in abeyance (Cushing's experiments).

The syndrome—adiposity, high sugar-tolerance, subnormal temperature, slowed pulse, asthenia, and drowsiness—has been attributed to a deficiency of the posterior lobe secretion.* The secretion of this lobe is thought to contain a hormone essential to carbohydrate metabolism,

FIG. 58.—Photograph of a well-marked case of acromegaly in a late stage. A. C., aged 40. There was a history of fifteen years' duration of the disease, of numbness in the hands followed by Marie's syndrome, of headaches, double optic atrophy and blindness, some adiposity, and towards the end uncinate symptoms, anosmia and loss of taste. (*By the kindness of Dr. Stebbing.*)

and it can easily be obstructed by various intracranial lesions. The emaciation,

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*Compare hibernation, with its low rate of metabolism, and its possible relation to seasonal pituitary variations.

"There can be little doubt that in the greater number of cases" of acromegaly "as the malady progresses, glandular insufficiency supervenes." Cushing's studies in carbohydrate tolerance show that "in acromegaly the individual's capacity to assimilate sugars progresses from a state in which carbohydrates are rapidly metabolized to one in which they are merely stored; in other words, from a state in which there is either a low assimilation limit or an actual hyperglycæmia with glycosuria, to one in which alimentary glycosuria is difficult or impossible to elicit. This would appear to be the strongest argument in favour of the transitional character of the disease from hyper- to hypo-pituitarism on which such great emphasis has been laid throughout this study."

"The transition doubtless may occur at the stage of the malady before the skeletal manifestations of hyperpituitarism have become outspoken, and thus the acromegalic changes may be inconspicuous (e.g., Case XII); or it may occur after the characteristic fixed bony changes have become full blown (e.g., Case XXVIII); or it may possibly not occur at all, and the disease may run a self-limited course after a stage of hyperpituitarism, with the restoration of a fairly normal glandular activity (e.g., Case XXXI)." (Cushing, *The Pituitary Body and its Disorders*, p. 251. The cases are Cushing's.)

spontaneous glycosuria with hyperglycæmia, and slight elevation of temperature which follow posterior lobe administration are in favour of this theory.

Glycosuria is so common at some time or other in acromegaly and giantism that according to Marie it is met with in one-third or one-half of all cases. It is probably connected with increased functional activity of the pituitary, but it is also suggested that it may have a cerebral (*see* p. 100) or a pancreatic origin. Falta[13] inclines to the latter theory because pancreatic atrophy has been noted in some cases. When the glycosuria occurs late in the disease, as in Mark's case, its hyperpituitary causation must be very doubtful.

Loss of Sexual Desire and Virility.—These are believed to indicate that the active or hyperpituitary stage of acromegaly has passed or is on the wane. Similar symptoms occur in other pituitary affections besides acromegaly, and in all they may be associated with atrophy of the testes. The interrelation of the pituitary and the testis will be apparent if the testicular functions are studied in conjunction with certain symptoms met with in the different pituitary affections.

Of the two functions of the testis, one—*the reproductive*—depends on the formation of spermatozoa in the seminiferous tubules, the other on the formation of a *supposed internal secretion* responsible for the secondary sexual changes that mark the onset of puberty. This internal secretion is believed to be produced by certain cells, known as the interstitial cells of Leydig, present in the intertubular connective tissue. Each function may develop alone, and when both have developed normally it is possible for recession to occur. The bearing of these facts both on acromegaly and on other pituitary disorders was illustrated by Cushing from cases reported in *The Pituitary Body and its Disorders*, and epitomized here :—

Case XLVII (Loc. cit., p. 224).—A boy, aged 8 years, acquired secondary sexual characteristics at 6—viz., masculine voice, axillary and pubic hair, and over-development of the genitalia. At 8 he was overgrown (5 ft. 6 in.), adipose, and blind. At the time of an exploratory cranial operation a small portion of the testis was removed for microscopical examination. The interstitial cells of Leydig were in excess, but the tubules were of pre-adolescent type, and without spermatozoa.

Case VIII (Loc. cit., pp. 63, 277).—A man, aged 41 years, "had never fully acquired the secondary characters of sex. He had a feminine type of adiposity and hirsuties, and so on ; nevertheless he had been sexually active. His testis showed fully developed tubular epithelium with spermatozoa, but there was a paucity of interstitial cells, none of which could be identified as cells of Leydig."

Case XXXII (Loc. cit., pp. 162, 277).—A giant, aged 36 and 8 ft. 3 in. high, presented the acromegalic peculiarities and had reached the stage of dyspituitarism. There was adiposity, increased carbohydrate tolerance, a childish voice, absence of axillary and pubic hair and of beard, small genitalia, atrophic testes, and he was impotent. Both spermatozoa and Leydig's cells were absent from the testis.

These cases are accompanied by confirmatory photomicrographs from sections of the testes in each.

The phenomena pointing to retrogression in adult acromegalics in whom the secondary sexual manifestations have already developed are less pronounced. Still, in the majority of cases the patient becomes aware of diminished sexual desire and of impotence. This feature is the more noticeable because in the early stage of hyperpituitarism an increase in sexual inclination is usually present. The transition may be illustrated by Cushing's Case I.

Case I (Loc. cit., p. 30).—A man, aged 35 years (December, 1910), was, at the age of 19, 6 ft. 4 in. high and of unusual strength. His habits were good except for an uncontrolled sexual desire. At 23 he had polyuria ; at 27 attacks of bursting frontal headache and pains in the extremities, followed by copious discharge of shiny mucus, which gave relief for days or weeks. Acromegaly was diagnosed at this time. In 1907 it had been noticed that his features were changing and that he was getting large all over. Polyuria without glycosuria was present, also weakness and drowsiness. He easily tired, and there was complete loss of sexual desire and power.

There can hardly be a doubt that the *amenorrhœa* of acromegalic women is to be explained in much the same way as loss of virility in men. The amenorrhœa of the declared disease is not difficult to understand, whether the theory of a deficient posterior lobe secretion is adopted, or a more recent hypothesis of pressure upon the basophil cells of the anterior lobe (*see* p. 99) as a cause of such deficiency is preferred. But why amenorrhœa should be the first symptom to mark the onset of the disorder is not very clear.

Pluriglandular Syndromes.—In addition to the signs which point to a derangement of the testicular functions in acromegaly, there are occasionally present, in some cases, symptoms which suggest that the secretions of certain of the other endocrine organs may be disturbed simultaneously with that of the pituitary. Of these, sweats, palpitations, nervous irritability, voracious hunger, tremor, and exophthalmos may be connected with over-activity either of the thyroid or the pituitary, but opinion hesitates as to which of the two glands is responsible. Reference has already been made (p. 77) to one explanation of exophthalmos, whilst Cushing attributes it to blood stasis from local pressure on the intracranial venous sinuses, and points out that it is present in almost all cases of tumour, and is rare in the absence of definite growth.

But the *thyroid* is undoubtedly affected in many acromegalics. In the 29 cases mentioned by Furnivall there were only 5 normal thyroids ; of the others, 17 were hypertrophied, and 7 showed degenerative changes. Cushing had rather a different experience : in 15 cases, in all of which there were signs of pituitary insufficiency, the microscope showed only excess of colloid and a low epithelium (functional involution). There had been no symptoms of hyperthyroidism in any of these cases, though possibly a hypersecretory stage of thyroid secretion might have passed unnoticed.

There is no doubt that thyroid deficiency is the cause of myxœdema when that condition is present in acromegaly, for it is relieved by thyroid and not pituitary tablets. In two cases of Hochenegg's the thyroids became permanently enlarged after extirpation of the pituitary, and after experimental extirpation of the pituitary definite changes, viz., cellular desquamation and hyperplasia, have been found in the thyroid (Cushing). It has been suggested that enlargement, such as occurred in Hochenegg's cases, may point to the thyroid assuming a compensatory rôle, which, as both the pituitary and the thyroid exercise an influence on bone growth (e.g., cretinism), is at least plausible.

Some clinical facts, however, give the impression that the same cause may excite both glands to over-action ; thus Falta's Case 30 developed a goitre simultaneously with acromegalic signs ; eventually Basedow's disease gave way to myxœdema. But Falta points out that myxœdema may also develop without signs of hyperthyroidism.

In some cases symptoms such as hairiness and pigmentation raise the question of implication of the *adrenals*. The following is an example (Cushing) :—

Case XXV.—A Hebrew, aged 40, had been developing acromegaly for six years. There was no adiposity, but an unusual degree of hypertrichosis. The coarse skin was mottled everywhere with a remarkable brownish pigmentation. Carbohydrate tolerance was not increased (limit for glucose 150 grm.). The thyroid was slightly enlarged and the testes were apparently unaffected. Cushing remarks of this case that " it represents a fairly recent and still active condition of hyperpituitarism. The extreme hypertrichosis* and excessive sweating were notable features. . . . The case serves as a fair clinical illustration of the pluriglandular nature of the malady. . . . In this patient furthermore there was an exceedingly low blood-pressure. This, with the pigmentation, hirsuties, and muscular weakness, suggested adrenal involvement."

It must be admitted that the above facts justify no very definite conclusions, but taken in conjunction with P. E. Smith's experiments and the observations of Cushing and Davidoff in the Rockefeller Monograph No. 22 they indicate a connection which future research will no doubt make plainer.

Fig. 59.—Lateral view of the Greenwich (acromegalic) skull. (*R.C.S. Stores.*)

THE BONE CHANGES AND THEIR PATHOLOGY

The process of ossification is normal, but the skeletal changes result from its exaggeration, and are almost certainly induced by an excess of the anterior lobe

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* Falta looks upon abnormal hairiness in acromegalics as an accentuated secondary sexual manifestation. (Loc. cit., p. 248.)

secretion. The uneven distribution of these changes may be explained by the influence of pressure and traction upon osteoblasts rendered hypersensitive by the hormone secreted by the anterior pituitary lobe. "Wherever there is traction applied by ligaments or by muscles, or pressure applied as in standing or walking, growth takes place in that part of the skeleton where the various forms of force act" (Keith[14]). A student making a not very critical inspection of an acromegalic skeleton might easily take it for one of a normal individual, unless, perchance, he got a lateral view, when he would be struck by the great depth of the chest, and the prognathous lower jaw (*Fig.* 59), provided these features were at all marked. But the difference between an acromegalic skeleton and a normal one becomes apparent when the measurements of corresponding parts are compared.

FIG 60—Side view of a normal skull (*R C S Museum*)

In the following table the measurements from the skull of a pronounced case of acromegaly (Dr. Corner's case, R.C.S. Museum, No. 3860.1) are contrasted with those from a normal Englishman's skull and with those of the skull of a man 6 ft. 3 in. in height in which the pituitary fossa was normal (Sir James Cantlie's specimen, R.C.S. Museum). (*Figs.* 60, 61.)

FIG. 61.—Skull of a case of acromegaly. Dr. Corner's case. Patient was a man aged 42, who had marked signs of the disease at 25 years of age. Height, 6 ft. ½ in. He was bedridden for his last ten and a half years. Some months before death there was improvement in intelligence, speech, and sight, which last had been seriously impaired. His hands and fingers became less (? spontaneous decompression into the sphenoidal cells—*see Fig. 57*). His bowels were relieved with great difficulty every seven days, and the rectum (preserved) is enormously enlarged and thickened, but is not a part of a general intestinal hypertrophy. The lungs were greatly enlarged, but there had been no lung affection at any time. (*R.C.S. Museum*, No. 3860.1.) *See also Figs.* 63, 67, 69, 70, 71, 73.

	ACROMEGALIC	NORMAL ENGLISHMAN	MAN 6 FT. 3 IN. HIGH
	Inches	Inches	Inches
1. From the root of the nose to the tip of the chin ..	7	5	5
2. Lateral oblique measurement; from the mid-point of the interparietal suture to the chin (tip) ..	11½	10	11
3. Circumference of skull ..	23½	21¾	22¼
4. Superior maxilla: orbital margin to alveolar margin	2⅜	1⅝	
5. Superior maxilla: width of palate area—between the last molars	1¾	1⅝	2
6. Length of hard palate* ..	2¼	2	1⅞
7. Mandible: depth of body	2	1¼	1¼
8. Mandible: width of arch between last molars ..	2¾	2	2⅛
9. Zygoma, length from the tubercle to the posterior vertical border of malar bone	R. 2⅝ L. 2½	2⅛ 2	2¼ 2¼

* According to Keith's observations the palatal area in the acromegalic is not increased.

In the following account of the changes which distinguish the individual bones in acromegaly, Sir Arthur Keith's explanatory description of those in the skull will be largely followed.

FIG. 62.—The normal and acromegalic mandible contrasted. The shaded areas mark deposited new bone. The stippled areas mark where bone has been absorbed. The thick outline ~~~~ ~~~ ~~~
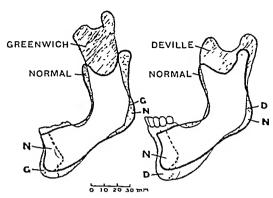
Normal; G, The Greenwich skull; D, The Deville skull. (*By the courtesy of Sir Arthur Keith, 'The Lancet', 1911, April 15, 996.*)

The Jaws (*Fig.* 62).—The alterations in the maxillæ and mandible are responsible for one of the most distinctive features of the affection. The heaping up of porous vascular bone on the alveolar margins increases the length of the face, raises the vault of the hard palate and the dental sockets, and separates the teeth.* This alveolar hypertrophy is to be attributed to the stimulation of bone growth by the intermittent pressure of mastication. The underhung and projecting lower jaw and chin, so characteristic of acromegaly, is explained by the changes that take place in the mandible. Besides the alveolar overgrowth, additional bone is deposited on the mental eminence and on the lower margin anterior to the groove for the facial artery. But the most interesting changes take place in the ramus, which becomes narrower and increased in height, sometimes more than one inch.

Absorption takes place in the region of the angle, producing the appearance of an opening out of the angle between the body and the ramus. The increase in height is due to growth taking place at the upper end. The condyle, the coronoid process, and the sigmoid notch form the growing portion, and pressure on the condyle, and traction on the coronoid process and

FIG. 63.—Cast of the face of Dr. Corner's case. (*R.C.S. Museum*, No. 3860.1.)

* Separation of the teeth is produced by elevation of the sockets; it is not due to an increased length of alveolar margin. The latter depends on the number and size of the teeth.

the notch constitute the stimulus to growth. By the growth at the joint the mandible is pushed downwards and forwards, and a misfit between the upper and lower teeth is the consequence. The narrowing of the ramus is explained by muscular traction, which is exerted more and more in the line of the ascending ramus, as the mandible is elongated and depressed by the growth at the joint. The wider separation of the angles may in part be connected with the increased size of the tongue. It is brought about by absorption on the inner side of the bone, and deposition on the outer side. The absorption and deposition of bone is like that which fashions a bone in ordinary growth, and they involve both the cancellous and cortical tissue. At first the new bone is porous, but later becomes condensed. Only occasionally, and in some places, does the bone deposit approximate to the inflammatory type.*
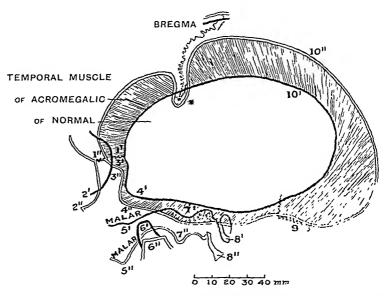
FIG. 64.—Comparison of the normal origin of the temporal muscle and boundaries of the temporal fossa with those of the acromegalic. 1′ External angular process of the normal skull; 1″ Of the acromegalic; 2′, 2″ Lower margin of orbit; 3′, 3″ Ascending process of the malar bone; 4′, 4″ Upper margin of the zygoma; 5′, 5″ Origin of the masseter (lower margin of malar); 6′, 6″ Coronoid process; 7′, 7″ Articular eminence; 8′, 8″ Tympanic plate; 9′ Parieto-mastoid suture; 10′, 10″ Temporal ridge (muscular). * Stephanion. (*By the courtesy of Sir Arthur Keith, 'The Lancet', 1911, April 15.*)
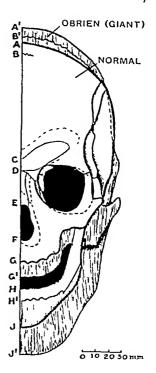
The Face (*Fig. 63*).—The study of the facial alterations must begin with the growth changes that occur in the temporal fossa and temporal muscle in the normal child. These are continued and exaggerated in acromegaly. As the attachment of the temporal muscle grows upwards, backwards, and forwards the temporal ridge

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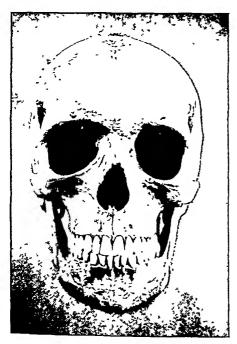
* Similar changes occur in some other conditions, but they are very rare. The following instances may be cited; (1) Hypertrophy of the right half of the lower jaw reminiscent of the acromegalic deformity is seen in Sir Jonathan Hutchinson's specimen from Mr. J. E. Adams' case of "Osteomata on the Interior of the Cranium and Nasal Fossa" (R.C.S. Museum, No. 1362.2, *Trans. Pathol. Soc. Lond.*, 1871, xxii, 204). (2) A cast in the R.C.S. Museum (No. 38.2) illustrates Mr. Barwell's case of a boy aged 7, in whom there was congenital hypertrophy of the bones of the right side of the face. The hypertrophy of the jaw was strictly limited to the right half. The soft parts and the right half of the tongue shared in the hypertrophy (*Trans. Pathol. Soc. Lond.*, 1881, xxxii, 282).

recedes. The key to the overgrowth of the supra-orbital ridges, and to the expansion of the frontal sinuses in acromegaly lies in the anterior region of this advancement and recession, i.e., in the displacement forwards of the anterior part of the temporal ridge. The abnormal temporal development produces a forward growth of the outer orbital region. "The external angular process with the ascending malar process comes to

FIG. 65—Half the full face of ....O'B..... compared with the normal. A, plane of orientation (subcerebral of vault above the plane of orienta B, Bregma, normal; Б', O'Brie , . ' , Tip of nose; F, Nasal spine; G, Alveolar point, normal; G', Ditto, O'Brien; H, Alveolar point of lower jaw, normal; H', Ditto, O'Brien; J, Mental eminence, normal; J', Ditto, O'Brien. (*By the courtesy of Sir Arthur Keith, ' The Lancet ', 1911, April 15.*)

occupy a position 10 to 15 mm. further forwards and downwards than in the normal skull ", with the result that the zygoma is lowered, the height of the temporal fossa is increased, and the external auditory meatus is depressed—in some cases 10 mm. or more. (*Fig.* 64.) Again, the supra-orbital overgrowth displaces the root of the nose forwards and downwards, so the nose appears to be long. It is also conspicuous, as the overgrown

FIG. 66—Front view of a normal skull. (*R.C.S. Museum.*)
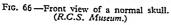
FIG. 67.—Front view of an acromegalic skull. Dr. Corner's case. (*R.C.S. Museum, No.* 3860 1.)

supra-orbital region predominates over the maxillary part of the face which is not projected more than usual. The increase in the face-length in a well-marked case is about 20 mm.; that of the upper face (10 to 17 mm.) being chiefly due to the increase in depth of the alveolar margin of the maxilla. (*Fig. 65.*)

In the front view two alterations call for notice. The first concerns the orbit, whose outer wall is moved forwards and outwards so that the orbits are enlarged outwards and downwards. The second is the remarkable enlargement of the malar and zygoma, the depth of the body of the former being increased as much as 8 to 15 mm. The orbital enlargement is a consequence of the temporal changes, and that of the malar and zygoma of the traction exerted by the masseter. (*Figs. 66, 67.*)
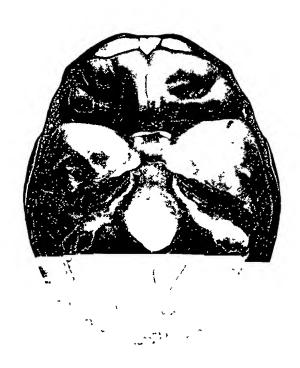
FIG. 68.—The base of a normal cranium. (*Osteological Collection, R.C.S. Museum*)

The Cranium (*Figs.* 68, 69, 78–80).—The modifications of the vault are not nearly so distinctive as those of the jaws, the supra-orbital ridges, and the face. Its thickness varies a good deal. Beadles[15] has recorded the case of an insane woman aged 40 years in whom the cranial vault was remarkable for its thinness and its large frontal sinuses (*see Fig.* 79). Most acromegalic calvaria are thicker than normal, and in rare instances they may be so thick as to resemble the vault in osteitis deformans (*see Fig.* 80). In some cases both tables are defined, but in others they cannot be differentiated from the dense diploë.

The frontal bone is the first part to be affected and undergoes the greatest amount of change, and in many there is a tendency to the formation of small dense

osteomata on its inner table. Posteriorly, the superior curved line with the occipital protuberance is moved upwards from 8 to 10 mm., and the distance between the mastoid processes is increased from 10 to 25 millimetres. Both these changes are due to the increased area of attachment of the neck muscles.

The Base.—The foramen magnum is displaced backwards in giants and forwards in adult acromegalics, a peculiarity explained by the increased length of the basilar process in the former and its atrophy in the latter. The occipital condyles may be reduced in size and their axes altered, so that the head is carried in increased

Fig. 69.—Base of an acromegalic cranium showing erosion and deformation of the pituitary fossa and its vicinity; expansion of the frontal sinuses, atrophy of the basi-occipital, and alteration of the foramen magnum. Dr. Corner's case. (*R.C.S. Museum*, No. 3860.1.)

extension. In some cases they may be pressed upwards more into the skull, as if the base had been softened. In Dr. Corner's case they are surrounded by considerable lipping, and in one of the Greenwich skulls (R.C.S.) (*see Fig.* 78) an atrophied axis is ankylosed to the occipital bone.

The Pituitary Fossa.—In nearly all cases there is some enlargement of the sella. In some it is inconsiderable, and occasionally it does not exceed normal limits; but in others the fossa is much increased in size, and in the worst examples the landmarks may be lost in the irregular cavitation of the sphenoid caused by tumour erosion. (Cushing's three types have been described on p. 78).

All the veins in and below the base dilate, especially the emissary veins. The small venous foramina open out, and one of them, the cranio-pharyngeal canal, may become patent.* The cranial capacity may be slightly increased, but the evidence on this point is inconclusive. That of the giant O'Brien (R.C.S. Museum) is only 10 c.c. more than the mean of a normal English skull.
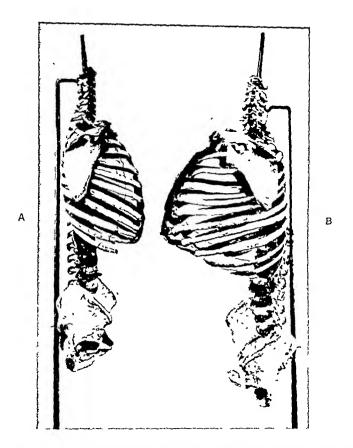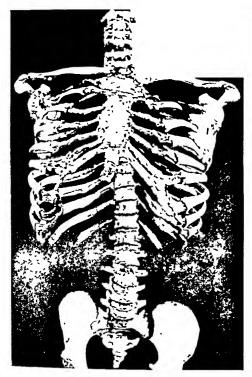
FIG. 70.—A normal, and an acromegalic thorax viewed from the side. A, Normal; B, Acromegalic. Dr. Corner's case. (*R.C.S. Museum, No.* 3860.1.)

The Thorax and Shoulder Girdle (*Figs.* 70–72).—The great size of the chest is very striking. It is largely due to the increased length of the ribs, especially of the middle ones, which carry the lower part of the sternum unduly forward. Its width is emphasized by the over-long clavicles. These points are well brought out in the illustrations, but will be even better appreciated from the comparative measurements (Dr. Corner's case).

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* Keith points out that in anthropoids it remains open and that it is present in O'Brien, in other giants, and in many acromegalics, but he explains it by a dilatation of a normal minute vascular channel and not as a congenital persistence betokening an inherent defect in the pituitary.

ACROMEGALY

	Acromegalic	Normal Englishman	Man 6 ft. 3 in. high (R.C.S.)
	Inches	Inches	Inches
Circumference of thorax over inferior angles of scapulæ and 4th rib	45	33	36
Length of clavicle	8	6¼	6⅜
Length of ribs (5th and 7th, R. and L.)	17½	13	14
Width of 1st rib (R. and L.)	1⅜	⅞	1
Depth of chest, xiphoid to spine	9⅜	6½	6¾
Transverse diameter above 6th rib	13½	9	9½

The ribs are unusually wide and the increase in their length is much greater than any seen in other long bones (excluding giantism). The length-growth is determined by several factors, viz., the permanence of the costal cartilages which

FIG. 71.

FIG. 72.
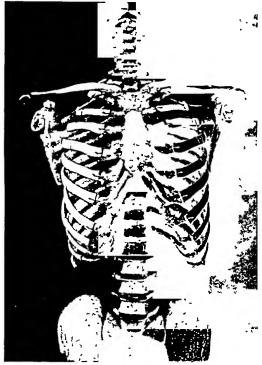
FIGS 71, 72.—Front views of thorax and spine. *Fig.* 71, Acromegalic. Dr. Corner's case (*R.C.S. Museum, No.* 3860 1). *Fig.* 72, Normal.

are elongated, hypertrophied, and irregularly calcified, the exaggerated growth processes, *and, last but not least, the hypertrophy of the lungs.* Their increased width

is due to the traction of the intercostal and chest muscles. The cartilages appear to penetrate the ends of the ribs, which are slightly expanded as if to receive their articulating portions. At this point, microscopically, a young layer of bone lies over the growing cartilage.*

The clavicles are rounded, thicker, less curved, and longer than usual, and the muscular grooves and ridges are abnormally developed. The increased growth in length is often remarkable, and no doubt partly the result of traction at their outer ends, called into play by the outward pressure of the expanding thorax.

The Long Bones.—Apart from the clavicles and ribs, the long bones may not differ very obviously from normal ones. The shafts are usually smooth and formed of compact bone, though they may be pitted and marked by vascular foramina and impressions. The articular ends are apt to be notably more massive and less elegantly modelled than usual. The rough areas and ridges associated with muscular and ligamentous attachments—such as the linea aspera, deltoid tubercle, etc.—are commonly exaggerated, and may, like the articular margins, be beset with small bony excrescences and rugosities. In many cases where there is no question of giantism the limb bones are not only thicker and more massive but may be increased in length—especially the humerus and femur. Nor is it difficult to understand this increased length-growth and massive bone-ends, even when the epiphysial lines have long been closed, if it is appreciated that growth can be determined in acromegaly by pressure and traction (compare the mandible).

The Bones of the Hand and Foot (*Fig.* 73).—The metacarpals, metatarsals, and the phalanges are not much altered. Sometimes their length is increased (Marie's long hand), but instead of being elongated they may be thick, rounded and massive, and the attachments of the aponeurotic flexor sheaths marked by sharp hypertrophied ridges. Small lateral exostoses on the shafts may be present, and the articular ends frequently show hyperostosis and lipping, suggestive of osteo-arthritis, a condition that not infrequently complicates the main affection.

FIG. 73.—The skeleton of an acromegalic foot. Dr. Corner's case. (*R.C.S. Museum*, No. 3860.1.)

* A very full account of the histology of the rib cartilage in the normal subject and in acromegaly, with the changes occurring at the chondro-costal junction, is given by Erdheim, " Die Lebenvorgänge im normalen Knorpel und seine Wucherung bei Akromegalie ". There are a number of illustrations.

A costal cartilage grows from its periphery (perichondrium) towards its central axis. The zone of proliferating cartilage lies parallel to the long axis of the cartilage, and not transversely as in the epiphyses of the long bones. A calcified layer is not developed on the deep or central border of the proliferating zone, but the vitality at this part begins to wane and the cartilage dies. The central core of a rib cartilage is composed of dead tissue.

The Vertebral Column.—The hypertrophic changes in the vertebræ may in some instances be of an osteo-arthritic nature, but Erdheim,[16] who has carefully investigated them, believes that there is a *true acromegalic spondylitis*. He points out that the changes affect the dorsal region in greatest measure, and tail off in the cervical and lumbar regions. They are due to the deposit of new periosteal bone upon *the diaphyses*—a deposit which is thickest in front, diminishes at the sides till it disappears, and is absent in the spinal canal. The margins of this partial bone sheath are fissured, so that a row of tooth-like processes appears above and below a vertebral disc. The overgrowth considerably increases the antero-posterior diameter of the body, and, if looked at from above, its shape is in marked contrast with that of a corresponding normal or osteo-arthritic vertebra.

In osteo-arthritis, on the other hand, the hypertrophic changes occur at the edge of what represents *the epiphyses* and are more irregular in their distribution (osteophytes). When exuberant they give a waist-like appearance to the diaphysis in which the surface of the normal body is exposed covered only by the periosteum.

Kyphosis; *Flat-foot.*—A cervico-dorsal kyphosis (spondylitis muscularis) and flat-foot are frequent concomitants of acromegaly. They are no doubt chiefly due to the failure of muscular tone and power which characterize its later stages. Atrophic changes in the vertebræ may be a factor, but deterioration of the muscular power is probably the main one.

Acromegalic Arthritis.—Erdheim's[17] researches show that a specific form of arthritis may occur in acromegaly. He points out that in osteo-arthritis the changes in the articular cartilage depend on degeneration. They begin at the surface, and extend deeply until the cartilage may be completely destroyed. In

Fig 74 —Section of a phalangeal joint and adjacent portions of the phalanges from an acromegalic old man (70 to 80 years). Showing the atrophic changes in the bone. (× 4)

acromegaly the exact opposite occurs. The changes result from exaggerated proliferation starting in the proliferation zone in the deep layers of the cartilage. As the proliferating focus advances towards the surface, its overlying normal cartilage is thinned by the pressure, and softened by the proximity, of the proliferating tissue. The covering layer is worn through by friction and the proliferating nodule or focus exposed. The edges of the ulcer are at first undermined, for crevices form between the passive and the proliferating cartilage as the latter increases. The presence of this undermined edge is characteristic of the acromegalic ulcer of articular cartilage, and when it disappears owing to the continued rubbing, it is very difficult to distinguish the acromegalic from an osteo-arthritic lesion.

Bone Atrophy.—Not only does absorption go hand in hand with bone growth in the evolution of the bony changes, but in the later stages of the disease, bone atrophy may be marked and extensive (*Fig.* 74). Evidence of this can be seen in skulls (*see Fig.* 79) and in the vertebræ (*see Fig.* 71, in which osteo-arthritis is present); but it may proceed to such lengths that a long bone may be converted into a cylinder of compact tissue with almost complete disappearance of the cancellous structure (*Fig.* 75).

Histology of the Process of Ossification.—The most helpful account is that of Marie and Marinesco,[18] who state that there is no essential difference from normal ossification. The proliferated cartilage cells, however, are arranged in irregular groups instead of columns, and these groups are separated by a considerable width of matrix. The line of junction of the cartilage and bone is festooned and irregular. The medullary spaces are rich in vessels and young cells, and vascular cell buds advance from them into the calcified matrix between the cell groups. The cell groups open into the spaces, and primary medullary spaces are formed, upon whose boundaries laminated bone is laid down by apposition of osteoblasts. In the diaphysis of the bone examined (middle phalanx of the great toe) resorption was going on, but osteoclasts on the trabeculæ were rare.

Under the periosteum, both layers of which are thickened, fresh layers of bone are produced, but they are disposed more irregularly than usual. The periosteal fibres play the same rôle as the calcified cartilage between the cell groups, i.e., as directing strands for ossification.

FIG. 75.—The anterior half of the right femur of an acromegalic giantess of 26½ years (height 7 ft. 8½ in.). To show the atrophy of the cancellous and cortical bone. (*Through the courtesy of Professor Brash.*)

The marrow in the later stages is often fatty, as might be expected, but Hunter,[19] in a man who died from cerebral hæmorrhage in the fifth year of his acromegaly, has described increased vascularity of the marrow and cancellous tissue of some of the long bones, and markedly red diploë in the cranial bones; whilst in the bones adjoining the pituitary fossa the marrow was of a deep plum colour; moreover, there were hæmorrhages in the medullary tissue of the tibia and the femur. The pituitary was enlarged, highly vascular, and red, in marked contrast to a normal pituitary. These changes were no doubt associated with active hyperpituitarism.

PATHOLOGY OF THE CHANGES IN THE SOFT TISSUES OF THE ACROMEGALIC PARTS

The soft tissues of a great toe were also investigated by Marie and Marinesco[18] (*Fig.* 76).

In the skin the various layers of the epidermis were thickened, the papillæ enlarged and elongated, and the derma proper was remarkably hypertrophied. Its thickness was 150 mm., whereas in portions of normal skin it measured from 0·5 to 0·7 mm. It was composed of thick bundles of connective tissue with hypertrophied fibres running parallel to the axis of the bone, and others obliquely and perpendicularly to the bundles. On its deep surface its vessels were thickened by cells concentrically arranged.

The adipose layer of the subcutaneous tissue was loaded with fat, and the connective tissue strands radiating from the aponeurosis and periosteum were two or three times thicker and more numerous than usual. The vessels were sclerosed, and in some the internal coat was so hypertrophied as to narrow the lumen.

The small nerve-sheaths were hypertrophied, the septa between the nerve-bundles thickened, and in the nerve-fibres the nuclei of
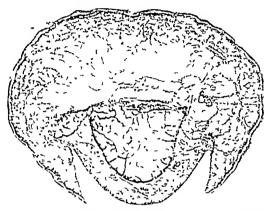
FIG. 76 —Transverse section of an acromegalic great toe showing thickened epidermis, dermis excessively hypertrophied, and composed of thick bundles of connective tissue, thickened Malpighian layer, hypertrophied strands of connective tissue which radiate towards the deep face of the dermis, walls of vessels thickened, thickened periosteum, enlarged medullary spaces (× 2) (*After Marie and Marinesco,* "*Arch de Med exper*", Fig 6, p 545)

the sheath of Schwann were multiplied, and many had lost their myelin. There was both peri- and endoneuritis. The peripheral nerve and vascular changes, as a rule, occurred only in the parts affected with acromegaly.

Hypertrophy is also met with in the *cranial, spinal, and sympathetic nerves.* Thus in Henrot's case the pneumogastrics, the glossopharyngeals, and the brachial plexuses were notably increased in size, and a life-sized drawing testifies to the remarkable enlargement of the main sympathetic system, with its ganglia and branches.

SPLANCHNOMEGALY

Cushing and Davidoff,[20] from observations made from forty-four completely recorded autopsies, "infer that the tendency to a disproportionate and widespread enlargement of the viscera is generally speaking a definite characteristic of the disease". The one exception is the brain, whose weight is ordinarily within normal limits. Cunningham's[5] case is a good example. The liver weighed $7\frac{3}{4}$ lb., more than twice its usual weight; the kidneys were nearly three times the ordinary weight and apparently quite healthy; the spleen weighed 14 oz. The stomach and intestines had attained a wonderful capacity; the former was four to five times the size of the ordinary stomach; the small intestine, when inflated, measured

37 ft. 3 in. in length, and the large intestine 11 ft. $\frac{1}{2}$ in. The whole intestine from pylorus to anus was little less than twice as long as in the ordinary male subject. Other well-known cases in which splanchnomegaly was present are Henrot's (liver, spleen, kidneys, and sympathetic system) and Neal's (liver, spleen, kidneys, heart, and thyroid). The hypertrophy frequently involves only some of the organs. In Dr. Corner's case there was marked hypertrophy of the lungs, in which there was no emphysema. The overgrowth had evidently been subjected to considerable restraint by the enlarged and capacious thorax. A most unusual and deep moat-like sulcus encircled the upper lobes just below the apices, a proof of sustained expanding pressure against the first ribs (*see* p. 91).

PATHOGENESIS

The pathogenesis of acromegaly and giantism is closely connected with the physiological functions of the cells that compose the anterior lobe of the pituitary body.

In the normal pituitary the anterior lobe is surrounded by a connective-tissue capsule, and columns or masses of cells are separated into variously shaped alveoli by connective-tissue strands, supporting blood-vessels. (Dean Lewis—Bohn and Davidoff[21]). The cells are not all alike, and can be differentiated by their peculiar reactions to different stains. One kind, known as *chromophobes*, does not stain with eosin or osmic acid, but takes only a slight yellowish tint. These cells are small. Another kind consists of large coarsely granular cells, styled *chromophils*. The granules in some take up an acid and in others a basic stain. These cells used to be classified, according to their reaction to eosin and hæmatoxylin, into acidophils and basophils; but as the acid and basic dye theory proved faulty, Dott and Bailey[22] preferred to use a non-committal designation for the stained granules. To the eosinophilic granules which stain with eosin, acid fuchsin, neutral dyes, etc., they applied the term ' *alpha granules* ', and to the basophilic granules, which stain with alum hæmatoxylin, kreso-fuchsin, acid-violet, etc., the term ' *beta granules* '.*

The two kinds of chromophil cells are distributed indiscriminately about the gland, but the cells of the pars tuberalis, which constitute the stalk, are mostly basophils. According to one view, there is really only one kind of anterior lobe cell, the different types marking different functional stages. Benda[23] thought he was able " to follow satisfactorily the transitional changes from the empty chromophobe to the loaded eosinophil", and " that the *small* cells with few granules represented the indifferent embryonal forms capable of multiplying, and that the accumulation of granules in the dark cells (eosinophil) indicated the highest point of functional activity; and that, finally, the *large cells* with few granules resulted from a temporary or permanent cessation of function." On the other hand, it is suggested that the three types are quite independent.

As a result of experimental and clinical observations Cushing has ascribed a definite function to each variety of the chromophil cells : to the acidophil,

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* " Many synonyms exist for these cell types in accordance with theories of their staining reactions, or the varying views regarding their function. (1) Chromophobes—chief cells, reserve cells, siderophils, etc. (2) Chromophils : (*a*) Eosinophil—acidophil, fuchsinophil, oxyphil, etc. (*b*) Basophil—cyanophil, etc." (Dott and Bailey).

undoubted association with growth, and to the basophil a probable and intimate relation to the organs of reproduction and sex. He thinks that these vital functions are activated by separate hormones, which arise in the different forms of chromophil cells.

The Acidophil Cells.—These are specially associated with acromegaly and giantism. The enlargements of the anterior pituitary lobe found in these diseases show a large excess of acidophil cells which are grouped into considerable masses to form an adenomatous tumour (Schafer[24]).*

This association is supported by certain very suggestive facts :—

1. Partial extirpation of such an adenomatous tumour has been followed in many cases by rapid amelioration of the symptoms ; and in one case (Hochenegg's) gradual diminution in size of the enlarged extremities set in and complete cure eventually resulted.

2. In young animals growth is checked when the anterior lobe is removed.

3. Giantism has been produced in a rat by repeated injections (parenteral) of saline emulsion of fresh bovine anterior lobe tissue (Evans and Long, 1921[25]).

The following account of the *histology of acromegaly* has been given by Dean Lewis.[26] The patient from whom the material was obtained was a man of 46 who died from cerebral mischief unconnected with his acromegaly. For nearly seven years his feet, hands, and head had been gradually getting larger, but post mortem the pituitary was not noticeably enlarged. There was, however, a notable hyperplasia of the chromophil cells. These rested directly upon the endothelial walls of the capillaries instead of on connective-tissue strands which support the bloodvessels and normally limit the alveoli. The cells were irregularly grouped in the inter-capillary spaces. Lewis describes two kinds of chromophil cells. The granules of the predominant cells—large polyhedral cells (*Fig.* 77)—stained best with iron hæmatoxylin (acidophils). Very few chromophobes and cyanophil (basophil-hæmatoxylin) cells were found, and they were grouped about the boundary zone between the nervous and glandular lobes. He regarded the great excess of highly functioning chromophil elements, their irregular distribution, and the lessened amount of stroma, as indicating excess of function, and he came to the conclusion that this cell hyperplasia was the fundamental change in acromegaly, because he had seen similar appearances in other acromegalic cases, and they were not present in several pituitary glands taken without discrimination from different cases.

The absence of pituitary enlargement, as in Lewis's case, is not very common in acromegaly—more often the gland is increased in size and assumes the tumour formation, especially in those that call for operative interference. Bailey and Cushing,[27] who examined a large number of pituitary tumours (from 100

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* *Pregnancy cells.*—Probably not unconnected with the ' acidophil cells ' are certain large granular or fibrillated acidophil cells (siderophil—$\sigma i \delta \eta \rho o \varsigma$, iron), which have been observed during pregnancy to form masses within the pars anterior. This is always enlarged at those times. They have been termed ' pregnancy cells ', and after parturition they diminish in size and lose their specific appearance (Schafer).

" *The chromophil adenoma.* The eosinophilic tumour. This adenoma is the form which accompanies the hyperpituitary syndrome. . . . As a rule these adenomata are of the strumous variety with scant connective tissue, and they are prone to cystic degeneration. In our experience tumours of this type are constantly associated with the syndrome of overgrowth, i.e., acromegaly or giantism." (Dott and Bailey : material from 39 cases was examined.)

consecutive cases, which included others besides acromegaly), made further valuable observations. They described six different histological types :—

1. In this type practically all the cells were packed with alpha granules.

2. Most of the cells contained large numbers of alpha granules.

3. Only a ring of alpha granules occupied the periphery of a variable number of cells.

4, 5, and 6. No alpha granules were present.

When they compared these types with the clinical conditions connected with them, it was found that the highly acidophilic adenomata (1 and 2) were *always*, and the pure chromophobe adenomata (4, 5, 6) *never*, associated with acromegaly (if two doubtful cases in type 4 were excepted). In the third or intermediary

FIG 77 —Portion of a section cut from the pituitary body of a case of acromegaly. Stained with iron hæmotoxylin (Leitz Obj. 12, Ocular No. 4). (*By the courtesy of Dr. Dean Lewis*)

type, in which sparsely disposed cells contained a peripheral zone of alpha granules, clinical evidence of a fugitive hyperpituitary reaction was apt to be present; the microscopical appearances* were characteristic of a class of case in which there was a synchronous development of the acromegalic and hypopituitary syndromes. Thirteen such cases from 162 verified adenomata were classified by Dott and Bailey as belonging to a 'mixed type' with dyspituitary syndrome. Bailey and

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* Dott and Bailey[22] give four coloured drawings illustrating : (a) The normal histological appearance of the anterior lobe ; (b) Crowded 'alpha' granules (Nos. 1 and 2) ; (c) Chromophobe adenoma (Nos. 4, 5, 6) ; (d) Adenoma with mixed clinical syndrome—cells outlined by a ring of 'alpha' granules (No. 3).

Cushing christened this clinical condition belonging to the third or intermediary type '*fugitive acromegaly*'.

The Basophil Cells.—These are thought, by those who advocate this theory, to secrete a hormone capable of activating the reproductive organs. This belief is based upon the following facts. The results of experiments seem to justify the presumption that the increased lustfulness, and the exaggeration of the secondary sexual characters such as hairiness, seen in the hyperpituitary stage of acromegaly, may depend upon the basophil cells of the anterior lobe (Engle,[28], Teel[29]). That an active sex substance exists was shown by Zondek and Aschheim,[30] who demonstrated its presence in the urine during pregnancy; and at the autopsy of a case with exaggerated sexual characters Teel found a small basophil adenoma of the pituitary—till then an unknown form of pituitary tumour.[25]

Again, certain circumstances suggest that the secretion of the sex hormone may be interfered with by pressure upon the basophil cells. Thus, suprasellar lesions producing a chiasmal injury with little or no enlargement of the fossa may be due to several kinds of tumour, one of which is the chromophobe type of pituitary tumour. In such cases the function of the anterior lobe is not interfered with, and no amenorrhœa results. But if a growing chromophobe tumour is confined within the sella, amenorrhœa invariably occurs. The same effect is no doubt produced by a *chromophilic* tumour in acromegaly, for the sex function is definitely interrupted when the pituitary fossa is greatly expanded by intrasellar pressure (Henderson[25]). On the other hand, " partial extirpation either of a chromophobe or an acidophilic adenoma in women " may result in the resumption of normal menstruation, and even in the occurrence of child-bearing.

Though it may be stated with some confidence that acromegaly depends upon the circulation of an excessive secretion of a growth hormone resulting from a hyperplasia of the acidophil cells of the anterior lobe, there is, at the present time, a clash of experimental evidence as to the seat of the influence that controls the sexual functions, notwithstanding the arguments pointing to the basophil cells. It has been located by Camus and Roussy,[31] whose results were confirmed by Bailey and Bremer,[32] in a group of nuclear masses in the tuber cinereum. They found that extirpation of the pituitary *in a dog* did not cause atrophy of the external genitals if the brain was not damaged, and, further, that after extirpation sexual vigour was preserved, and pregnancy was followed by the birth of living pups, which the bitch suckled for several days. On the other hand, genital atrophy, or at least arrest of development and loss of sexual appetite, resulted from experimental lesions of the base of the brain.

The inference from these results was qualified by those of P. E. Smith,[33] whose hypophysectomized *rats** showed pronounced retrogression and atrophy of all the reproductive organs; and as these parts were restored by replacement therapy (daily pituitary transplants) he concluded that the atrophy was due to the removal of the anterior lobe, and not to brain injury.

Adiposity, High Sugar Tolerance, and Polyuria.—These have been attributed to a deficiency of the posterior lobe secretion, probably resulting from

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* Owing to the similar disposition of the dural diaphragm in rats and man, in whom it is only perforated for the passage of the stalk, the gland below, and the nerve structure above, can be separately subjected to experimental injury.

atrophy of that lobe from the pressure of the pituitary tumour, or from obstruction to the outflow of the secretion owing to compression of the stalk. Doubts, however, arose when Ashner[34] suggested that the polyurias, glycosurias, adiposity, and general atrophy that followed extirpation of the pituitary in dogs might be caused by incidental damage to the tuberal nerve centres; and the doubt was increased when, in the light of their experimental results, Camus and Roussy concluded that these symptoms were in all probability the result of injury to the adjacent nerve centres in the floor of the third ventricle, and these comprised a group of nuclear masses believed to control the metabolic and sexual functions in the normal animal.

FIG. 78.—Base of the Greenwich (acromegalic) skull. Compare with *Fig. 69*. Note the exostoses on the internal table and the different shape of the foramen magnum. (*R.C.S. Stores*)

Important evidence in support of this view was furnished by the work of Richter and of P. E. Smith. The former produced a persistent polyuria in a series of animals by a carefully placed stab-wound through the bases of rats' skulls just anterior to the pituitary, and the latter contrasted two experimental procedures. In one, by the ventral route, he extirpated the pituitary by negative pressure (suction), easily permitted by its anatomical disposition in the rat, and in the other, using the temporal approach, he injected chromic acid into it. In the latter experiment the caustic effects might be expected to extend beyond the limits of the pituitary body. The symptoms that followed were similar except as regards

obesity. The rats in which the chromic acid method was used developed an early and unusually marked adiposity, whilst those in which the pituitary had been removed showed none or only a slight obesity after five or more months.

These researches have cast considerable doubt upon the 'hypopituitary syndrome' theory, and Cushing admits that they have badly shaken " our accepted views of the relation of these symptoms (polyuria, adiposity, sexual dystrophy) to the pituitary body itself". In the Lister Memorial Lecture Cushing gives the impression that he has in his mind the idea that eventually it may not be impossible to harmonize to some extent the contradictory results of the different experimenters, and that deficiency symptoms may prove in some cases to be caused by interference with nerve-fibres which run from the supra-optic and paraventricular nuclei down the stalk to ramify in the posterior lobe round the secretory islands, or possibly by damage to the blood-supply to the gland as it passes along the infundibulum.

Changes in the Thyroid and Adrenals.—In both sets of Smith's experiments there invariably resulted atrophy or involution of the thyroid, and retrogressive changes in the cortex of the adrenals. The nature of the changes in the various ductless glands has been carefully discussed by Cushing and Davidoff in the Rockefeller Monograph No. 22, to which the interested reader is referred. They conclude their study of the thyroid with the following sentence : " We may, nevertheless, safely say that hyperpituitarism in its acromegalic guise tends to enlarge the thyroid disproportionately to the other tissues, and that this enlargement proves, histologically, in the large majority of cases, to be the type of the inactive gland familiar in the colloid goitre." Concerning the adrenals, they say, " evidently hypertrophy of the adrenal cortex, with or without the formation of adenomata, is one of the most constant expressions of hyperpituitarism."

ETIOLOGY

What is the cause of the excessive secretion of the anterior pituitary lobe which is thought to be the effective factor in the production of acromegaly ? It is not certainly known, but it is conceivable that the increased secretion may be due to abnormal stimulation or abnormal sensitiveness of the gland. The excitant may possibly be a hormone originating in some physiological process, or a toxin connected with some bacterial infection. Its origin may be still more complicated, and the following considerations may have some relation to the problem.

Pregnancy.—During pregnancy the pituitary body increases in weight and size, and changes from a greyish-red colour to white. It subsides after parturition, and involution is complete at the end of lactation. With a succeeding pregnancy a further enlargement takes place. In the anterior lobe " the acidophil cells no longer dominate the field ", but are crowded away from the sinuses, which they once lined, by neutrophilic cells derived from the normal chromophobes. " It is many months after parturition before the acidophils regain their former predominance " (Erdheim and Stumme[35]).

Though these changes are very different from those seen in acromegaly, there is some clinical evidence to support the suggestion that the short-lived pituitary hyperplasias of pregnancy may precede the onset of acromegaly. The sequence occurred in two of Cushing's cases (Cases II and XXIV), and the acromegalic signs

were followed by those of hypopituitarism. Moreover, the association with pregnancy is very clear in Marek's case in which transitory acromegaly developed during gestation in a 27-year-old primipara. The nose and jaws became larger and the teeth spread apart, the tongue increased in circumference, the tonsils swelled, and glycosuria, lassitude, and insomnia were present. All the signs disappeared during the puerperium (Falta[36]).

The relationship of pregnancy to pituitary conditions is further elaborated in the following quotation from *The Diseases of the Pituitary Body* (p. 235): "repeated involutions from the chromophobe hyperplasias of the Erdheim and Stumme type
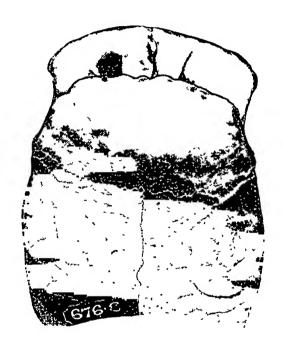
FIG. 79.—Anterior portion of an acromegalic calvarium, showing great enlargement of the frontal sinuses and thinning of the vault. From a woman, aged 40, who died in an asylum and who had shown marked signs of acromegaly for seventeen years. The body was very obese and the skeleton enormous. The thyroid was hypertrophied, and the kidneys and spleen greatly enlarged The pituitary body was converted into a large cystic tumour, and had produced a cavity in the sella turcica as large as a small hen's egg. Death occurred from hæmatemesis, which was due to capillary congestion of the stomach's mucous membrane (Dr. C. F. Beadles' case, *Edin. Med Jour*, 1898, 501) (*R C S. Museum*, *No. 3868.1*)

may bring about a physiologically inactive condition of the gland", bordering on the pathological, and so explain " a measure of hypopituitarism " and " account for the excessive adiposity, loss of hair, asthenia, subnormal temperature, and so on, not uncommonly seen in women after multiple pregnancies ".

Puberty.—There is no question that the increase of growth that occurs in adolescence is definitely associated with puberty, and the fact that giantism develops in adolescence naturally suggests testicular influence. The increased lustfulness

of the early stages of acromegaly again emphasizes the linking up of the testicular and pituitary functions. Rapid growth in adolescence is probably due to physiological pituitary hypersecretion, and the glycosuria met with at that period, and in pregnancy, may be similarly explained. In all individuals at such times carbohydrate toleration is probably low (Cushing). (*See* pp. 79, 80.)

Infection.—There is both experimental and microscopical evidence that the pituitary body is affected by bacterial intoxication. Clinically, the various infections that have preceded the onset of acromegaly are tubercle, obscure pulmonary trouble, typhoid, scarlet fever, and rheumatism. In Rodriguez's[37] case of a girl, aged 16 years, an acromegalic giantess, extraordinary growth began between the fourth and fifth years, and she had suffered from meningitis at the age of three. (*See also* Henrot's case, p. 70.)

Another interesting fact may be noted: that when pituitary manifestations arise after infection or traumatism, it is acromegaly that follows infection, and hypopituitary symptoms that follow trauma.

Heredity.—The occasional occurrence of giantism or acromegaly in a family in which there is a definite tendency to skeletal overgrowth in more generations than one suggests that sometimes there exists a familial proclivity to functional instability of the pituitary. Transition from a physiological disturbance to a pathological state would be more likely to take place in the presence of such a predisposition than when the pituitary is endowed with the normal power of resistance. In the former case the onset of acromegaly might be determined by puberty, one of the infections, or a pregnancy.

TREATMENT

The treatment of acromegaly will be considered under the headings of: (1) Irradiation; (2) Surgical interference; (3) Glandular therapy.

1. **Irradiation.**—The use of X rays and of radium are included under this term. Its object is to promote atrophy of the anterior lobe cells and shrinkage of the gland, or, short of that, a diminution of the functional activity of the cells.

The different kinds of cells vary in their sensitiveness to irradiation. The eosinophil (acidophil) adenomata are said to be " very radio-sensitive, and to respond to X-ray treatment almost immediately ", but " the chromophobe adenomata are radio-resistant, and while the increase of intracranial pressure can be reduced in these cases, the growth of the tumour cannot be influenced " (Kerley[38]).

The X rays and radium have each their appropriate place in treatment. The former can be used in the early stages of the disease by radiation from the surface, but the latter is unsuitable for surface radiation when the pituitary has to be attacked (Sargent and Cade[39]). It must be applied *in situ* in the form to be described below.

One of the earliest cases in which X rays were used was Beclerc's.[40] A young giantess, aged 16, was completely relieved in two months of severe headache, and the left field of vision was tripled after ten weeks' weekly radiation from the fronto-temporal region.

Similar cases have been recorded by J. H. D. Webster,[41] Teel,[29] and others. In these cases the X rays constituted the initial treatment, but they have also been used with advantage after operation. Frazier,[42] indeed, has employed both X rays and radium as a routine post-operative measure from 1917. In post-operative

treatment the rays are more effective if they are applied over the aperture in the skull.   Radiation by the rays is indicated not only in the hyperpituitary stage of acromegaly, but also when the hypopituitary syndrome is present, if it is thought that the tumour growth is causing pressure atrophy of the acidophil cells and so leading to deficient secretion.

When radium is used it is applied locally after the tumour has been exposed by operation.   The important structures in the immediate vicinity of the pituitary body are easily damaged, so the emanation from the element is preferred to pure radium.   The emanation—known as ' radon '—is contained in small platinum tubes called ' seeds '; its energy is at its maximum when it is first given off, and steadily diminishes till none is left.   The seeds, therefore, may be left *in situ* permanently.   On the other hand, ' needles ' contain small quantities of the actual element (radium dust), whose energy is perpetual—consequently needles must be removed.   In situations in the brain other than the pituitary they may be preferred to ' seeds '.   Two or three seeds are sufficient for insertion in a pituitary tumour, and as they have a tendency to fall to the bottom of the fossa they should be planted with care.   Further, the possibility of excessive dosage " producing permanent blindness " must be kept in mind (Sargent and Cade[39]).   Wakeley[43] has inserted nine radon seeds round about a pituitary tumour in a case of acromegaly in a woman aged 21.   The patient was said to be " perfectly well " five weeks later.

2. **Surgical Interference.**—Operative treatment may be necessary, some-times urgently so, to prevent threatened blindness or to relieve intense headaches. The intracranial symptoms are likely to be relieved, but the general signs are less influenced, though they may be improved.   An operation is indicated when a patient who presents Marie's syndrome, with increased sellar measurements, develops an increasing hemianopsia.   In most cases the proceeding adopted is the exposure of the anterior lobe or tumour by one of the several methods of approach, and the removal by curetting of a considerable proportion of the adenomatous or hyper-trophied gland, or the evacuation of a cyst.   Instead of partial removal, radon seeds may be inserted in suitable cases.   The improvement that follows is often striking; headache vanishes, vision and the visual fields improve, and the patient may be so much benefited as to be able to resume his occupation.   But this is not always the case, and blindness may be only postponed.   In some cases a bitemporal decom-pression may be thought the wiser course.

After many procedures have been proposed, and some carried out, three routes for reaching and exposing the pituitary have gradually become defined: (1) An extracranial or nasal route, known as the ' trans-sphenoidal'; and (2) Two intra-cranial routes—(a) the ' frontal ', and (b) the ' subtemporal '.

Frazier has laid down the following indications for deciding the choice (loc. cit., p. 223) :—

1. A simple decompression—subsellar (trans-sphenoidal route)—with incision of the capsule, is indicated : (a) When there is no striking evidence of intracranial extension (" Usually atrophy of the clinoid processes implies a rupture of the diaphragm, and an intracranial extension "); (b) " When there has not yet been a spontaneous decompression which results from erosion of the sellar floor."

2. The suprasellar or intracranial route is to be chosen : (a) When spontaneous decompression has already taken place; and (b) When there is positive evidence of intracranial extension.

He considers that the suprasellar operation is a much more formidable procedure than the extracranial, because it implies an attempt at a more or less radical extirpation of the lesion—a criticism that does not apply to the insertion of radon seeds—whilst " after the relief of pressure by a subsellar decompression the growth of the lesion may be arrested by the use of radium and X rays ".

Trans-sphenoidal Operation.—The following is a brief description of the trans-sphenoidal operation as described by Cushing.[14] " The upper lip is drawn up and the transverse incision first advocated by Halstead for hypophysial operations is then made across the labial frænum. The incision is carried down to the anterior nasal spine of the superior maxilla." The operation then resolves itself into a submucous one, with removal of most of the vomer, the lower edge of the median plate of the ethmoid, and a small strip of cartilage. The prow of the vomer underlying the sphenoidal cells is identified and possibly removed. The sphenoidal cells are easily recognized, and the anterior and lower walls chipped away with long-handled nasal rongeurs, the lining membrane removed, and the sellar protrusion exposed.

FIG. 80 —Transverse section through the parietal bones of an acromegalic skull resembling the cranium in osteitis deformans (Niccolucci). Natural size (R C S *Museum, No* 3861 1.)

The bone is easily chipped away, and the dural covering or capsule is opened with a knife hook, and a crossed incision made. Such a degree of extirpation as is considered advisable is then carried out. A head-lamp, special retractors, and speculum are necessary, and all oozing must be stopped as the operation proceeds, so that every step can be seen. Drainage, which was used at first, is now omitted, and the incision under the lip closed with two or three catgut sutures.

" The procedure is median from the outset ; it is conducted in favourable cases without entering the mucous-lined nasal cavity ; it can be carried out in one session, and is somewhat less mutilating " than some similar methods, as the turbinates are merely flattened temporarily, and not removed.

Any surgeon contemplating the performance of this operation for the first time should read Cushing's description, in which valuable hints are given as to the avoidance of the various difficulties likely to be met with.

The chief value of the trans-sphenoidal method lies in the subsellar decompression. The necessary limitation and uncertainty of the extirpation that can be carried out by it add to the difficulty and the risks of the operation ; and Frazier,[45] writing in 1928, states that notwithstanding the lower operative risk, it has been

abandoned in the Pennsylvania Clinic because recurrence of symptoms was not infrequent, and they had felt obliged to " adopt the transfrontal method as the procedure of choice."

Satisfactory results, however, may follow it, as a case reported by W. E. Saner[16], seventeen years after its performance, proves. The patient's vision was definitely improved and his strength recovered, and he had worked on a farm ever since. His appearance was strikingly acromegalic, but the circumference of his hands had diminished 1 in. and the size of his boots from No. 11 to 10.

Frontal Operation.—The frontal route is the simpler of the intracranial or suprasellar operations. It consists in an " incision from ear to ear across the vertex, and the scalp is pushed forwards over the supra-orbital ridges " (Wakeley). A large bone-flap is cut from the right frontal region, the dura mater is stripped from the orbital plates of the frontal bone, and then incised just in front of the small wing of the sphenoid. The frontal lobe is raised, and the optic nerves and chiasma, and the situation of the tumour, when it occupies the chiasmal region, exposed. The tumour is attacked above the chiasma and straight sinus. The operation is conducted from the right side, so that the left and more important frontal lobe is least disturbed.

Subtemporal Operation.—In the subtemporal operation the approach is made along the middle fossa. After the osteoplastic flap has been turned down the dura is opened and the temporo-sphenoidal lobe raised. There are important vessels, sinuses, and nerves to be avoided, but it may be preferable to the frontal route when the tumour occupies the interpeduncular region (Cushing). This was the method employed by Horsley.

3. **Glandular Therapy.**—The position of glandular therapy is not very assured, and so long as the true explanation of the hypopituitary syndrome is uncertain it must be regarded, to some extent, as an empirical method of treatment. Its results are not nearly so impressive as those obtained by thyroid feeding in myxœdema, or by the administration of insulin in diabetes. Frazier[47] had only three cases in his entire tumour series in which demonstrable improvement followed the ingestion of pituitary and thyroid extracts, but in all three the improvement was striking.*

Some judgement is necessary in the employment of the pituitary extracts. In the active state of acromegaly they would be likely to aggravate the symptoms, but when the pituitary secretion is failing and is deficient they may be used with some hope of improvement. In the latter case the whole gland extract should be given, because, when the pituitary is subjected to pressure, both lobes tend to be put out of action.

By such treatment, even though it makes but little impression upon the adiposity, the other pituitary symptoms may be distinctly benefited. " The body temperature is apt to regain its normal level, the blood-pressure becomes higher, constipation is less troublesome, and there is less drowsiness and often marked improvement in mental activity " (Cushing).

As an example of the kind of improvement that may be hoped for, the following case of Frazier's, in which a pituitary adenoma had been partially removed for

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* Frazier looks upon thyroid extract as an effective supplementary agent, as experimentally the interrelationship between the thyroid and pituitary has been conclusively proved.

headache and blindness, may be quoted: The patient presented many of the stigmata of pituitary dysfunction, including adiposity, no facial or axillary hair, pubic hair of the feminine type, and mental apathy. (No mention is made of any acromegalic signs*.) A year later headache was not so severe, but he was otherwise unimproved; cerebration was slower, and he slept most of the time. On Jan. 1, 1927, pituitary feeding of anterior and posterior lobes was begun (2 gr. night and morning). On Feb. 20 the patient, from a somnolent, almost comatose state, had become alert and able to get out of bed into a wheel chair. On Aug. 25 he could get about unaided, somnolence had completely disappeared, and, six weeks before,
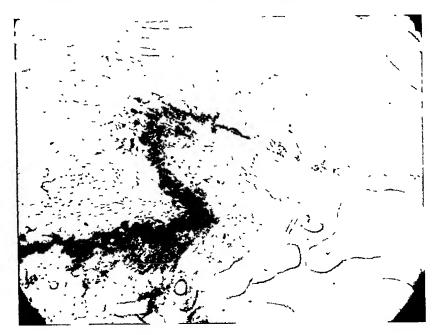
FIG. 81.—Transverse section of portion of the shaft of a phalanx from the same case as *Fig.* 74 showing a calcified projection into the periosteum (Ironside Bruce's node). Ossification has not advanced into the calcified mass from the cortical bone. (× 40)

he had had his first nocturnal emission. At this time he was taking 1 gr. each of anterior and posterior lobe and of thyroid extract twice a day.

A corollary to pituitary feeding would be *grafting* if that procedure were not too impracticable in the human subject to demand serious consideration. Cushing,[48] however, was once able to take advantage of opportunity, and records an instance in which the implantation of the hypophysis of a new-born child maintained an improvement of deficiency symptoms when it became impossible to continue injections of the whole gland, which had been giving considerable relief. The implantation was made in the subcortex of the temporal lobe at the site of the original decompression.

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* The reader is reminded that acromegaly is only one of several conditions associated with the pituitary body that may present the clinical features of the 'hypopituitary' syndrome. Probably the explanation of the symptoms is the same in all.

Most of the work upon glandular therapy is experimental, and the complexity of the physiological and pathological problems makes the subject rather bewildering.

In the preparation of this article much help has been given to me by many friends, and though in most instances it has been noted in the text, I desire here to express to them my grateful thanks, and especially to Sir Arthur Keith, the late Curator of the Royal College of Surgeons' Museum, Mr. T. W. P. Lawrence, Dr. Stebbing, Dr. Dean Lewis, of Johns Hopkins University, Professor Brash, of Birmingham, the Curator of St. Bartholomew's Hospital, and Dr. Frank Corner, whose interesting case is an important part of the groundwork of this paper. Nor must I omit to acknowledge the help derived from the MS. and complete bibliography which have been published in Mr. F. R. B. Atkinson's book on acromegaly. Three other friends, Dr. G. H. Rodman, Dr. C. F. Beadles, and Dr. Baly, to whom I have been indebted on this and many other occasions, passed away while I have been at work. Two of the illustrations in this paper are from Dr. Rodman's camera. Lastly, it is a pleasure once more to pay tribute to Messrs. George and Smith, and Miss Glasscock, of the College of Surgeons' Staff, to whose willing assistance the illustrations bear ample witness.

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PSEUDO-MYELOMATOUS   CARCINOMATOSIS

By L. COSIN

PRINCE OF WALES'S GENERAL HOSPITAL, LONDON

MARTIN, Dechaume, and Ben-Rais have drawn attention to the combination of multiple carcinomatous metastases in bone with Weil and Clerc's syndrome of splenomegaly and an anæmia, often hyperchromic, which is characterized by the presence of many immature red and white cells; there is rarely any great leucocytosis.

They describe the case of a woman, aged 54, who was admitted for widespread bony pains two years after a right radical excision of the breast for carcinoma. She was found to have splenomegaly and a hyperchromic anæmia, and radiograms showed the presence of many areas of rarefaction of bone, especially marked in the vertebræ. There were 1,580,000 red cells per c.mm., 37 per cent of which were nucleated; hæmoglobin was 37 per cent, giving a colour index of 1·18. Of 11,000 white cells per c.mm., 48 per cent were neutrophils, 15 per cent myelocytes, 15 per cent lymphocytes, and 22 per cent mononuclears. Post-mortem examination showed widespread replacement of the marrow spaces by new growth, and secondary deposits in ovaries, liver, spleen, and mediastinal glands. The close parallel between this case and that to be described will become apparent.

CASE REPORT

HISTORY.—Sidney C., aged 25, was admitted to hospital on Nov. 11, 1933, for pain and bruises, especially in the lower limbs, and great fatigue. There had been tenderness on pressure over the middle third of the sternum for the previous four months, and crops of petechiæ and bruises for the previous three months. Two months before admission the patient noticed severe throbbing pain in both lower limbs; this persisted for the next three weeks, and then moved to the shoulders, the right more than the left. As far as he knew he was apyrexial during this period. Much relief followed one week's rest in bed, but the symptoms rapidly became more marked on walking. He consulted his doctor, who was impressed by the pallor, enlarged spleen, and petechiæ. More recent symptoms were hæmorrhages from the gums and nose. The platelet count was later found to be 60,000 per c.mm. (Nov. 28). Winter cough and similar vague muscular pains, most marked in limbs, fingers, and shoulders, had been noticed for the previous four years.

ON ADMISSION.—The skin was of an earthy tinge, mucous membranes were pale, and there was little subcutaneous fat. There were a few petechiæ, most marked on the lower limbs, and a large superficial bruise was situated over a bony irregularity of the lower third of the right fibula. (There was no history of injury to this region.) The breath was fœtid, and the gums were soft and oozed blood. A few palpable lymph-glands in the right groin were not considered abnormal, but after the patient had been in hospital for eight weeks groups of mobile elastic glands suddenly appeared in both axillæ, groins, epitrochlear regions, and on both sides of the neck. The spleen was hard and uniformly enlarged down to the umbilicus. At no period of observation was the liver palpable. There was a soft apical systolic murmur, but the heart was otherwise normal, as were the respiratory and nervous systems. The optic discs were normal on admission, but, following a complaint of sudden mistiness of vision six weeks later, bilateral subhyaloid hæmorrhages were found, that on the right partially obscuring the macula. Normal gravitation occurred by the next day, leaving

the typical crescentic appearance, and vision improved simultaneously. Repeated urinary examination—especially for Bence-Jones proteose—revealed no abnormality. The skull and long bones were tender on palpation, and radiograms showed numerous circular punched-out areas of absorption of bone, all of approximately the same size and with very well defined edges (*Fig.* 82). This change was most marked in the skull, but could be seen in vertebræ, ribs, sternum, sacrum, ilia, and the bones of the limbs.
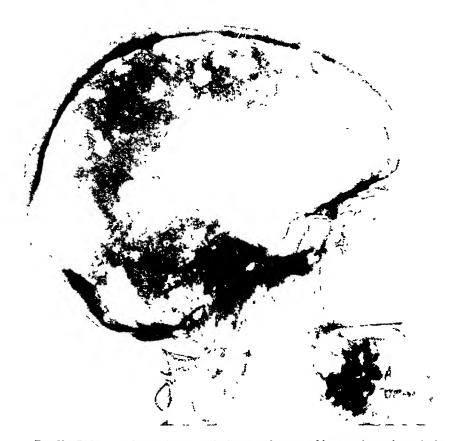
FIG 82.—Radiogram of skull showing multiple areas of erosion of bone, each circular with clear punched-out edges, some perforating only the inner or outer table, and others extending through the calvarium.

Investigation showed that the plasma phosphorus, serum calcium, and serum phosphatase were normal. The Wassermann reaction was negative in the blood, and the blood-urea, uric acid, and cholesterol were also normal. The blood-sedimentation rate, however, was 120 mm. per hour. On admission there was a mild anæmia (hæmoglobin 60 per cent, red cells 3,000,000 per c.mm., colour index 1) ; the reticulocytes were increased (8·6 per cent) ; and there were 15 per cent myelocytes with a rapidly rising white-cell count (*see Table*).

Upon this evidence a provisional diagnosis of myelogenous leukæmia was made and deep X-ray therapy applied over the spleen (Nov. 21). A severe reaction followed, during which the muscular pains became very much more severe, and were associated with headache, vomiting, and rigors. The pulse-rate rose to 120 per minute and the temperature to 104°. The phagocytic index showed that there were only 4000 actively functioning neutrophils per cmm. Deep X-ray therapy was, therefore, discontinued. The hæmoglobin fell rapidly

despite massive doses of iron and liver. There were repeated hæmorrhages from nose, gums, and bowel, rarely profuse and easily controlled.

A peculiar symptom was polyuria during the last few days of life, when the average daily output was above 100 oz. The patient died on Jan. 21, 1934, after ten weeks in hospital. During this period there had been persistent pyrexia ranging between 99°. and 101°.

RESULTS OF BLOOD EXAMINATION AT VARIOUS STAGES OF THE DISEASE

	1933 Oct. 25	1933 Nov. 12	1933 Nov. 28	1933 Dec. 5	1933 Dec. 11	1933 Dec. 31	1934 Jan. 1
Red cells (millions)	3·6	3·0	2·8	2·4	1·8	1·6	0·75
Hb (per cent)	65	60	48	38	34	23	10
Colour index	0·9	1·0	0·85	0·8	0·9	0·7	0·7
White cells (thousands)	10·6	20	5	3·6	3·0	3·5	2·3
Neutrophils (per cent)	40·5	45	45	40	42	41	16
Myelocytes (per cent)	17	15	18	7	3·5	4	6
Lymphocytes (per cent)	30·5	23	17	34	37	50	78
Mononuclears (per cent)	5·5	13	19	14	16	2	0
Basophils (per cent)	1	1	1	3	1	3	0
Eosinophils (per cent)	3·5	3	1	2	1	0	0

AUTOPSY.—Post-mortem examination was performed by Professor Nicholson, and revealed multiple subcortical hæmorrhages in the brain, particularly in the region of the optic chiasma. There was a hæmorrhage anterior to the left caudate nucleus and also into the right lateral ventricle. Many pinkish-yellow nodules in the meninges had produced regularly punched-out areas in the inner table of the skull. In several places these had extended through to the outer table so that there was continuity between the dura and the overlying aponeurosis of the epicranius muscle. Similar areas had partially eroded the outer table only, while erosive deposits were found in the spongiosa and cortex of every bone examined, the change being particularly marked in the proximal long bones. Several firm white raised nodules were found on the pleura, while there was marked peribronchial thickening in the lungs, which were slightly œdematous and emphysematous. There were several subpericardial hæmorrhages and white deposits in the myocardium. No deposits were visible in the liver, which gave a positive Perl's reaction. The spleen was much enlarged and studded with white nodules. Both kidneys had similar deposits and subcapsular hæmorrhages.

HISTOLOGY.—Histological examination of the tissues was made by Dr. Simpson, to whom I am indebted for the following report :—

" The masses of growth present in the peribronchial tissues, under the pleura, and in the spleen, kidneys, myocardium, brain, and bones consist of large ' oat-celled ' forms of an ill-differentiated carcinoma of the form now recognized as of bronchial origin. A tendency to differentiate in an ' acinar ' manner, a feature to which attention was drawn first by Turnbull, occurs in the masses lying in the lung tissues, but not in the more distant metastases. The latter are isomorphic with the oat-celled growth seen first and are clearly more primitive and rapidly growing, presenting frequent necroses, some with hæmorrhage. In the parts taken from the lungs no definite site of origin is suggested, as is, unfortunately, so often the case, but there can be no doubt as to the actual nature of the growth. The deposits in bone require special attention. These are multiple centred and histologically of great activity of growth, the bony lamellæ showing active resorptive processes without much osteoclast cell reaction. No myeloid reaction is present. The impression of a most fulminating metastasis is given, the marrow tissues being displaced with great rapidity, and showing evidence of but the slightest resistance. No unusual features accompany the infiltrations in the spleen or other organs. Those in the spleen are scattered and of varying size, being placed in the reticulum, massively in the sinusoids, and scantily in the outer ring of reticular cells around the Malpighian bodies."

COMMENT

The reactions of bone to secondary metastases can be subdivided into two main types depending upon the degree of malignancy of the primary tumour. Should this feature be relatively low, there will be a correspondingly slow rate of

growth, so that the surrounding tissues are sufficiently irritated to enable them to react. This 'osteoplastic' type is best exemplified in carcinoma of the prostate, where the diffuse reactive condensation of bone may result in obliteration of the marrow cavity. When the malignant deposits are subperiosteal, in which event they are grouped round the large issuing venous sinuses (von Recklinghausen), there will be a 'malignant periostitis', with the laying down of much new bone. When malignant disease of the kidney, breast, thyroid, or lung affects the skeleton, it is more often of a higher grade of malignancy. Growth is more rapid and the bone is destroyed so that the 'osteoclastic' or rarefying reaction is seen. It is in this type that spontaneous fracture and collapse of vertebræ occur.

In both types, however, should a sufficient amount of bone-marrow be destroyed, the mechanical replacement of hæmatopoietic tissue will result in a progressive anæmia with the presence of many immature red and white cells. It might be expected that some degree of thrombocytopenia would occur and that petechiæ and hæmorrhages might be noticed, as was found in some of Weil and Clerc's cases. This was not commented upon in the case of Martin, Dechaume, and Ben-Rais, nor was it found in a case of C. F. Cosin's in which a woman of 33, with diffuse osseous carcinomatosis, hypochromic anæmia, and splenomegaly, was found at autopsy to have primary carcinoma of the ovary with multiple splenic metastases.

It would appear, then, that the well-known immunity of the spleen to carcinomatous infiltration is not maintained when a growth proves capable of infiltrating myeloid tissue. In all these three cases bony metastases were associated with invasion of the spleen by growth.

The enlargement of the spleen (more rarely of the liver) may be due to the metastases in these organs or to a myeloid metaplasia, as was seen in the case of Martin, Dechaume, and Ben-Rais.

In the osteoclastic type, when there is no evidence of an obvious primary source, disorders of calcium metabolism, such as hyperparathyroidism, must be considered. These can be excluded by investigation of the calcium balance. Osteitis deformans rarely gives rise to difficulty in diagnosis. The most difficult differential diagnosis lies between multiple myelomatosis and carcinomatosis. The blood picture in multiple myelomatosis is so variable as to be useless in diagnosis. It has been variously described as being normal, showing a mild hypochromic anæmia, or frankly leukæmic in type, especially in the later stages of the disease. It is usuallys tated that the enlargements of the spleen and liver do not occur in multiple myelomatosis, although deposits may occur there before they are found in the bones, but it must be obvious that providing there is sufficient mechanical replacement of bone-marrow the typical picture of Weil-Clerc's syndrome will appear, whatever the cause.

Bence-Jones proteosuria occurs in only 65 per cent of cases of multiple myelomatosis (Copeland), but it also occurs in some cases of carcinomatosis. Thus the absence of this substance cannot exclude multiple myelomatosis, nor can its presence confirm. In fact Bence-Jones proteosuria is of less value in diagnosis than is Weil-Clerc's syndrome. Biopsy is an unjustifiable procedure when merely used to satisfy idle curiosity, nor is it entirely without risk.

Radiography has been previously claimed to be the only test which will clearly differentiate the two conditions (Sutherland, Decker, and Cilley), for it is said that it is only in multiple myelomatosis that the perfectly circular, clear-cut

punched-out areas of rarefaction occur. The fallacy of this assumption has been proved in this case. Enlargement of the lymph-glands does not occur in multiple myelomatosis; it does not occur as commonly as might be expected in carcinomatosis, although Copeland reports a case of carcinoma of the stomach in which the first symptom was a widespread enlargement of the lymphatic glands with a blood picture typical of Weil-Clerc's syndrome. In the present case this lymphatic enlargement appeared after the patient had been in hospital two months, and only two weeks before death. It should be realized that the only evidence of carcinomatosis may be Weil-Clerc's syndrome with no radiographical bony changes whatsoever.

SUMMARY

A case of pseudo-myelomatous carcinomatosis occurring in a man, aged 25, is described. This showed radiograms typical of multiple myelomatosis and the presence of Weil-Clerc's syndrome of splenomegaly and anæmia, often hyperchromic, with many nucleated red cells and myelocytes. The total white count was rarely above normal. The importance of this syndrome in the diagnosis of carcinomatosis is stressed.

Other peculiar features of the case were the terminal polyuria, which might have been due to invasion of the pituitary or hypothalamic region, the difficulty of diagnosis even at autopsy, and the occurrence of splenic metastases. The frequent impossibility of differentiating between multiple myelomatosis and carcinomatosis without biopsy is pointed out. In both this case and that of Martin, Dechaume, and Ben-Rais, a high mononuclear cell-count was present.

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OMENTAL TORSION WITH UNUSUAL SYMPTOMS

By C. R. SALSBURY, Kingston, Ontario

OMENTAL torsion is not so rare as was previously considered, and reports of cases are becoming increasingly common. The time may be already reached when publication of cases for statistical purposes only is no longer justified. The following cases are recorded, however, because in one the diagnostic problem was one that has not, so far as could be discovered, been previously reported.

Case 1.—A male, aged 57, was admitted to the Salford Royal Hospital because of abdominal pain. This was felt first in the epigastrium, but shifted to the right iliac fossa in approximately twelve hours. He had vomited twice in the twenty-four hours since the onset, but there had been no bowel movement. Examination revealed the scar of an operation for inguinal hernia on each side, tenderness in the right iliac fossa, a dry tongue, temperature 98·2°, pulse 84, and respirations 24.

A diagnosis of acute appendicitis was made and operation performed. The appendix was normal but was removed. The operation report states: " Torsion of greater omentum present; excised," but there is no description.

Case 2.—E. J., a well-developed boy of 9 years, was admitted to the Salford Royal Hospital, under Mr. E. D. McCrea, on Aug. 14, 1933. He complained of pain in the right side of the abdomen, beginning during the afternoon of Aug. 12. According to his story he had spent the afternoon at a football match, and a lady had leaned against him, with her elbow against his abdomen, during most of the game. He ascribed his pain to the pressure of her elbow. As he did not eat much that night, he was given a laxative. On the following day he ate a good breakfast went for a walk, ate again at noon, but refused the night meal. There was one bowel movement with no complaint of pain.

During the afternoon of Aug. 14, he again complained of pain, and lay with his thighs flexed. He was seen by his physician and sent to hospital. There had been frequent urination for the two days preceding his admission.

Fifteen months before this he had had fifteen teeth removed because of ' stomach trouble ' of many months' duration. This had not troubled him since the extractions. He had had mumps at the age of 3, chicken-pox at 4, scarlet fever at 5, and whooping-cough. His mother, father, and only brother were in good health.

ON EXAMINATION.—Examination, except of the abdomen, was of no importance. Temperature, pulse, and respiration were normal. The most prominent finding was a greatly distended bladder. Catheterization was performed and 20 oz. removed. Urinalysis revealed nothing abnormal. With the bladder empty, a large mass could be felt in the right side of the abdomen. It extended up to the liver and down to the anterior superior spine. (Note made at the time, " Probably an appendicular abscess, but very high.")

Aug. 15.—He required catheterization in the morning and evening. The mass was smaller in the morning, but definitely larger in the evening. Because of the position of the swelling and its variation in size, hydronephrosis was suspected and cystoscopy decided on. The white-cell count was 16,000. Differential not done.

Aug. 16.—Cystoscopy by Mr. McCrea. The bladder held 4 oz. without discomfort. There was a little débris, but the mucosa appeared normal. The left ureteric orifice was prominent, but the right was small and seen only with difficulty.

After the intravenous injection of indigo-carmine the dye appeared in seven minutes from the left ureter and flowed freely. None had appeared from the right side in fifteen minutes. A ureteric catheter was inserted into the right ureter and fluid came freely but without any trace of dye. The catheter was left in place. The urine from the right kidney showed red and white blood-cells, but not in sufficient number to be of any diagnostic significance.

Aug. 17.—"Abdominal mass varies in size, but has not disappeared."

Aug. 18.—The ureteric catheter was removed. There had been no further change in size.

Aug. 25.—Uroselectan was given intravenously. Both kidneys showed up well. There was slight enlargement of the right ureter and renal pelvis. The size of the swelling had not altered.

Operation was decided on. A note made before operation presents the following summary: "For hydronephrosis: normal temperature; dilatation of right ureter and pelvis; the sudden onset; location of the mass and its variations in size. Against hydronephrosis: failure to disappear after ureteral catheterization; the acute retention; the X-ray appearance which, although showing some dilatation, certainly was not that of a hydronephrosis of sufficient size to produce the abdominal swelling."

OPERATION (Aug. 30, Mr. McCrea).—A low oblique incision was made just medial to the right anterior superior spine, so that the kidney, ureter, or abdominal cavity might be explored. As soon as the muscles were divided it became obvious that the mass was intraperitoneal, and the peritoneum was opened in the line of the incision. A very tense, shiny mass, about 3½ in. in diameter, appeared in the wound. This occupied the right inferior part of the greater omentum, which was twisted into a rope of approximately 5 in., the end nearer the tumour being much more tightly twisted than the central end (*Fig.* 83). The direction of rotation was clockwise and there were two and a half turns. There were light adhesions to the anterior abdominal wall. These, obviously, must have occurred after torsion. Numerous enlarged lymph-glands were scattered throughout the mesentery of the small bowel and there were some in the omentum itself. They were neither caseous nor calcified. The twisted omentum was ligated in sections and cut through, and the abdomen was closed with a small drain to, but not through, the peritoneum. The wound healed by primary union.

The von Pirquet skin reaction was negative and no history of tuberculosis could be obtained for any member of the family.

On first getting out of bed the boy walked with the typical gait of flexion contracture of the right hip. This seemed to be due to a fear of extending the

thigh, as there was no limitation of passive movement and no paralysis. The limp gradually disappeared, and when discharged on Oct. 2 he was walking quite normally. He has been seen several times since and is perfectly well.

DISCUSSION

Acute omental torsion is by no means rare. At least 225 cases have been recorded: Morris[1] 217, Jeffries[2] 4, D'Errico[3] 2, and the present 2.

Case I presents nothing new, but illustrates two very common findings—that a previous operation for hernia is a very strong predisposing factor and that the usual pre-operative diagnosis is acute appendicitis.
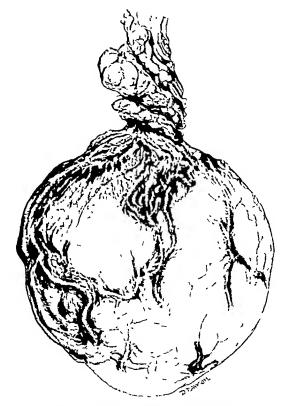
FIG. 83.—*Case* 2. Torsion of the omentum.

Case 2 is of much greater interest. According to the classification of Morris, this is an acute unipolar torsion, complete and without hernia. Of the reported cases with sufficient data to classify, 22 per cent are of this type.

The pathological diagnosis, unfortunately, cannot be unequivocally stated. Microscopic examination showed a thick fibrous wall with no evidence of tubercle formation but without an endothelial lining. The contents were thick, homogeneous, practically colourless, with no caseation, necrosis, or hæmorrhage. The glandular enlargement suggests tuberculosis, but the negative skin reaction is

interesting.   Taking all things into consideration, however, we feel that the condition was tuberculous.   Is this the real explanation of his symptoms of fifteen months previously ?

This seems to be the fifth youngest case on record, there being one of 3 years, two of 5, one of 7, and this one in a boy of 9.   In young children omental torsion is much more likely to be due to cyst than is the case in an adult.   A cyst was found in the child of 3 and in one of the 5-year-old cases.   The specimen in this case was actually a cyst, whatever its etiology.

The case was admitted to hospital as a probable acute appendicitis.   This is the most common diagnostic error, occurring in 60·02 per cent of all cases in which the pre-operative diagnosis was given.   As already described, later developments suggested a hydronephrosis.   We have failed to find a record of any other case with urinary symptoms.

The frequency of urination during the first few days and the slight dilatation of the right ureter and pelvis were probably due to the direct pressure of the tumour.   Or was it retention overflow ?   The acute retention is much more difficult to explain.

The apparent variation in size of the palpable swelling was probably rather a variation in tension, the result of partial untwisting and retwisting.   It is interesting to note that this occurred only during the first few days, giving us a reasonably reliable guide to the date of the formation of the adhesions to the anterior abdominal wall.

SUMMARY

Two cases of acute omental torsion are recorded.   One case showed several interesting and unique features leading to difficulties of diagnosis, and we have attempted to explain these in terms of the lesion found.

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STRANGULATED INTERNAL HERNIA:
REPORT OF CASES OF STRANGULATION IN THE FOSSA ILIACO-SUBFASCIALIS AND THROUGH THE FORAMEN OF WINSLOW

By G. F. LANGLEY

SENIOR RESIDENT OFFICER, THE GENERAL HOSPITAL, BRISTOL
LATE RESIDENT SURGICAL OFFICER, THE ROYAL INFIRMARY, BLACKBURN

ONLY three cases of hernia into the fossa iliaco-subfascialis of Biesiadecki are mentioned in the literature, and the records of these are indefinite. The following case of strangulation of ileum in this rare fossa appears worthy of record. The second case, strangulation of jejunum in the lesser sac of peritoneum, is less rare, but exemplifies the occurrence of double intestinal obstruction so accurately described by Finsterer.[1]

CASE REPORTS

Case 1.—Strangulation of ileum in the fossa iliaco-subfascialis of Biesiadecki.

HISTORY.—Mrs. Rachel H., aged 70, was admitted to the Blackburn Royal Infirmary on June 9, 1933. For four days she had complained of severe colicky abdominal pain in the umbilical region; vomiting had been almost continuous since the onset, and had been fæculent for over three days. For three days there had been absolute constipation, and three turpentine enemata had produced negative results.

For the past three months there had been fullness and discomfort in the umbilical region shortly after meals, which had sometimes been relieved by vomiting. The patient's bowels had been opened every second day after taking liquid paraffin, and neither blood nor mucus had been noticed in the stools. She had seven children and there was nothing of note in the gynæcological or urinary history. For many years she had suffered from severe chronic bronchitis and œdema of the feet.

ON ADMISSION.—The patient was gravely ill, the tongue was dry and furred, the skin was dehydrated and inelastic. Temperature 98°, pulse 106, respirations 36. Fæculent material was vomited twice during the examination. The abdomen showed central distension, the flanks were flat, and peristalsis was seen and heard across the umbilical region. A deeply placed, ill-defined mass was detected in the right iliac fossa, the percussion note was resonant, and there was marked tenderness and some muscular guarding in this region.

DIAGNOSIS.—A pre-operative diagnosis was made of: (1) Gall-stone ileus; (2) Carcinoma around the ileocæcal valve; (3) Appendicitis causing lower ileal obstruction. It was decided to perform an emergency ileostomy under local anæsthesia.

FIRST OPERATION (June 9).—After preliminary saline infusion the abdomen was opened through a small gridiron incision in the right iliac fossa under novocain anæsthesia. The ileum was greatly distended and the cæcum was empty; a tender fixed mass was felt below the cæcum in the iliac fossa, but the patient was *in extremis* and it was not explored further. A Witzel type of ileostomy was performed just proximal to this mass and a No. 12 catheter was inserted.

Post-operative Course.—This was satisfactory; free drainage occurred from the tube and the patient's condition improved rapidly. After thirty-six hours the tube was clamped intermittently and a turpentine enema following upon an injection of pituitrin produced the passage of flatus. On June 12 the tube was clamped most of the day and preparation was made for a barium X-ray examination on the following day to guide in further treatment.

On the evening of June 12 the patient had a recurrence of her previous symptoms; greenish fluid was vomited several times and no drainage could be obtained from the ileostomy tube even after gentle irrigation.   I concluded that either the tube had become dislodged or
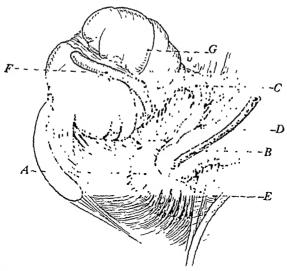
FIG. 84.—Sketch of hernia into fossa iliaco-subfascialis showing condition at operation. The cæcum and ileocæcal valve are retracted upwards to expose the iliac fossa and the hernia which is in the middle thereof.   Shiny peritoneum covers all structures except the catheter. *A*, Hernia elevated above the iliac fossa, plum-coloured and covered by peritoneum; *B*, Dilated proximal ileum; *C*, Empty lower ileum; *D*, No. 12 rubber catheter entering proximal ileum at hernial orifice; *E*, External iliac vessels; *F*, Appendix lying free over cæcum; *G*, Under surface of cæcum (lifted up).

else it had caused a kinking with secondary obstruction, and, as the patient was in a rather better condition, decided to explore under spinal anæsthesia.
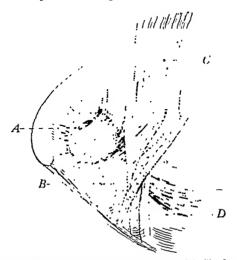
FIG. 85.—Diagrammatic representation of hernial sac in middle of right iliac fossa—bowel not shown. *A*, Slit-like orifice of hernial sac; *B*, External iliac vessels; *C*, Psoas magnus muscle; *D*, Pelvic cavity.

SECOND OPERATION (June 12).—Through a right paramedian incision the ileum and jejunum were seen to be distended, but the cæcum and lowest 4 in. of ileum were collapsed. The ileostomy tube was in the lumen of the bowel, but its tip was fixed inside a plum-coloured

mass on the posterior wall of the iliac fossa into which the distended ileum and collapsed lower ileum were seen to enter. This mass, the size of a tangerine, was separated by 2 in. of parietal peritoneum from the peritoneal ligaments of the cæcum, but the fundus of the cæcum almost reached its upper portion; its outer edge was 1½ in. internal to the anterior superior iliac spine, while its inner edge reached nearly to the outer border of the psoas muscle.

The orifice of the hernia was on the upper internal aspect and the tip of the catheter was seen to be inside the distended proximal ileum entering the sac. The peritoneum over the sac was non-adherent and was incised, but the hernia was seen to have occurred deep to the iliac fascia of which a thick band across the neck of the sac had to be cut before the bowel was liberated. Four inches of ileum had been strangulated but were viable, a recent constriction groove was seen across the end of the catheter, and a roughened annular patch 1½ in. distal to this suggested the presence of an older constriction groove which might have been the cause of the earlier strangulation. The ileostomy commenced to drain well and the boundaries of the sac were investigated.

The neck of the sac consisted of a slit-like band of iliac fascia, and its anterior wall was formed of this structure. It was lined by parietal peritoneum through which, on the deep surface, the iliacus muscle fibres were seen. The outer border of the psoas muscle was palpable by the finger inserted into the sac. Two catgut sutures closed the sac, and the wound was sutured, leaving the ileostomy tube protruding from the original incision.

Post-operative Course.—The patient recovered well, and after clamping the catheter intermittently after the thirty-sixth hour it was removed on the eighth day. The wounds healed well, and the patient was discharged from hospital three weeks later.

Case 2.—Double intestinal obstruction due to stenosis of colon with hernia of ileum through foramen of Winslow.

HISTORY.—Thomas K., aged 70, was admitted to the Blackburn Royal Infirmary on Jan, 1, 1934. For six hours he had complained of intense colicky central abdominal pain and frequent vomiting; there had been no bowel action for two days, and no flatus had been passed for the preceding six hours.

A left inguinal hernia had been present for years, but had given rise to no trouble. Two years previously he had been admitted to another hospital suffering from " ulcer of the stomach ", and after X-ray examination had been treated by diet and medicine for four weeks. He had not been improved by this treatment, and for the past two months had suffered from colicky umbilical pain and vomiting after food without relief of the pain. The bowels had become increasingly constipated for three months, and increasing doses of aperients had been necessary to obtain an action every third day. No blood or slime had been detected, and he had lost weight rapidly.

ON ADMISSION.—The patient was gravely shocked; temperature 95°, pulse 92. The skin and subcutaneous tissue was dehydrated, the vomitus was copious and of a dark coffee-ground nature. A vaginal hydrocele was found in the left side of the scrotum, but there was no hernia. The abdomen showed a very obvious distension above the umbilicus, reaching on the right side nearly to the costal margin and on the left to beneath the ribs. This region was very tender, there was some muscle-guarding, and the percussion note was resonant. There was a visible and palpable ballooning of the cæcum, and an ill-defined swelling in the region of the pelvic colon was noted. Rectal examination was negative.

DIAGNOSIS.—A pre-operative diagnosis was made of strangulated paraduodenal hernia with a probable concomitant colonic obstruction due to carcinoma of the pelvic colon. The epigastric swelling seemed to be the cause of the acute symptoms and might account for the previous ' gastric ' history if it were a long-standing internal hernia; the history of increasing constipation and the ballooned cæcum suggested a more chronic colonic obstruction. It was therefore decided that this might be an example of double intestinal obstruction as described by Finsterer, and preparation was made for the performance of an ileostomy as in the previous case. While preparation was being made in the theatre for this to be done under local anæsthesia the patient vomited copiously and died.

AUTOPSY.—There was gross distension of the lesser sac of peritoneum, and the gastro-hepatic omentum was œdematous and infiltrated with blood. A loop of jejunum, 2½ ft. long, was found to have entered through the foramen of Winslow and was tightly strangulated in the lesser sac. The bowel appeared to be non-viable. The cæcum was ballooned with gas to about 7 in. in diameter and the ascending and transverse colon were distended. The whole

pelvic colon showed extensive intramural fibrosis, narrowing the lumen to the size of a quill. There were several inflamed diverticula and many pericolic adhesions, but no carcinoma was present. The fæces were hard and black owing to a bismuth mixture ordered by the patient's doctor, and there was obviously a colonic obstruction due to the fæcal impaction above the stenosed colon. There had thus been a definite double intestinal obstruction; the large internal hernia had probably been present for years causing mild symptoms, and the onset of strangulation had been accelerated by the development of a subacute obstruction of the colon causing increasing distension of the jejunum. There was no ulceration of the stomach or duodenum, and the gall-bladder was healthy.

THE PARACÆCAL HERNIÆ

Moynihan[2] collected and described all available records of paracæcal herniæ up to 1906, and, including these, I have been able to collect 42 cases from the literature. The site of the hernia has been as follows, using the classification of Moynihan and Rendle Short[3]:—

1. Hernia into the ileo-appendicular fossa   10
2. Hernia into the retrocolic fossa 23
3. Hernia into the fossa of Hartmann   2
4. Hernia into the fossa iliaco-subfascialis, including case of hernia
     of appendix described by Mott   3
5. Hernia into lateral cæcal fossa, described by Rendle Short .. 1
6. Hernia into anomalous openings 3

The anatomy of these fossæ has been described in great detail in Lord Moynihan's book and that of the last two types has been detailed in the various papers.

The Fossa of Biesiadecki (Iliaco-subfascialis).—This fossa is also called the subcæcal or iliac fossa or the fossa infracæcalis by various writers. It is situated in the middle of the iliac fossa and its size varies from a small transverse slit to a large fossa 2 in. in diameter with a wide elliptical mouth. The orifice is directed upwards and is bounded in front by a fold of iliac fascia running towards the iliac crest. Biesiadecki[4] demonstrated that the fascia in the upper half of the iliac fossa is lax and freely movable upon the iliacus muscle, whereas that in the lower half is more firmly bound down. Tarenetzky[5] showed that the junction of the two is often marked by a sharp upwardly concave fold, and further that this fossa can exist on either side of the abdomen.

I have dissected this region in a large series of autopsies and have been unable to demonstrate this fold of Tarenetzky in most, but when it has been present I have always found that the psoas parvus muscle has been exceptionally well developed. The psoas parvus is present in 45 per cent of people and is inserted into the fascia at the level of the ilio-pectineal eminence, from which strong bands of fibrous insertion radiate fan-wise towards the anterior superior iliac spine, Poupart's ligament, the posterior lamella of the femoral sheath, and also gain direct attachment to the ilio-pectineal eminence via the ilio-pectineal septum, which passes between the psoas and pectineal muscles. I have seen a well-marked fold of Tarenetzky in nine cases and on each occasion have noticed a very strong fascial insertion of the psoas parvus muscle, which has been the direct cause of the fold, passing towards the anterior superior iliac spine. I have demonstrated this point in a full-term fœtus in which bilateral folds were present associated with bilateral psoas parvus muscles, but in another fœtus in which there was a unilateral psoas parvus muscle the

fold was present only on the side of this muscle. The development of the fossa iliaco-subfascialis would therefore seem to be dependent upon the presence of a strong psoas parvus muscle whose fibrous insertion into the anterior superior iliac spine gives rise to the fold of Tarenetzky.

Hernia into the Fossa of Biesiadecki.—Moynihan quotes two cases. One is that of Engel, who found this hernia incidentally in a man who had died from pneumonia. Engel's description is: " The cæcal pouch was dilated so as to contain the small intestine with the exception of the upper portion of the ileum. The orifice of the sac admitted two fingers. As this sac was developed wholly in the right half of the abdomen the cæcum was pushed above and to the left of the umbilicus, and the colon and sigmoid flexure were pressed to the left. The intestine was distended with gas but could be removed from the sac quite easily and could be easily replaced." Moynihan, commenting on this description, says that it is "meagre and insufficient". Engel describes it as a case of retrocæcal hernia, but Moynihan agrees with Leichtenstern in regarding it as a case of hernia into the fossa iliaco-subfascialis.

The second case quoted by Moynihan is that of Mott, who showed the specimen to the London Pathological Society. " The vermiform appendix measured 7 in. It turned up behind the cæcum forming a sigmoid band, and terminated in a peculiar pouch 1½ in. long in the anterior part of the iliac fossa. This pouch has been described as the infra- or retro-cæcal fossa. Mr. Treves termed it the fossa iliaco-subfascialis. There was apparently a small artery running along the pouch."

The third case, not described in Lord Moynihan's work, was one of strangulation of ileum in this fossa and was operated on by Mr. Dunn at Guy's Hospital. It is referred to in Rowlands and Turner's *Operations of Surgery*,[6] but unfortunately no further details are available.

The case described here would therefore appear to be the only detailed record of a strangulated hernia into the fossa iliaco-subfascialis. The case of Engel appears to belong to the category of arrested rotation of the gut and to be rather of the nature of a congenital malposition as described by Edmund Andrews[7] than a genuine example of acquired hernia into this fossa.

SYMPTOMATOLOGY AND DIAGNOSIS

1. Cases with No Symptoms.—Many cases of internal hernia have been found at autopsy or during laparotomy for other lesions where there have been no symptoms referable to the hernia.

2. Cases with Chronic Abdominal Symptoms.—Several cases of paracæcal hernia have been found during operation for chronic appendicitis (Atherton[8]) and recurrent colic (Rock Carling and Jones,[9] Coley and Hoguet[10]). Both the patients described in this paper gave a history of gastro-intestinal symptoms which might have been due to distension of the bowel within the hernia without actual strangulation.

3. Cases of Strangulation.—Most cases have been discovered during operation for an acute abdominal lesion; the correct diagnosis is rarely made.

In the table on p. 124 my case is included as intestinal obstruction.

CASES PRESENTING ACUTE SYMPTOMS (27)

Diagnosis
- Appendicitis 6
- Ovarian lesion 1
- External hernial strangulation 2
- Labour pains 1
- Intestinal obstruction 16
- Paracæcal hernia 1

A palpable mass has been noted in cases described by Riese,[11] and by Mansell Moullin,[12] and in my own. Coley and Hoguet, however, found a swelling in a chronic case of retrocolic hernia which they diagnosed.

Moynihan groups the symptomatology as follows: (1) Acute strangulation; (2) Recurrent subacute obstruction; (3) Palpable tumour formation—(a) The swelling is localized to a definite region, (b) Gurgling peristaltic sounds are often heard over the tumour, (c) The size and tension of the swelling are increased when strangulation occurs.

The obstruction in all cases is in the small gut, and pain is thus of a colicky nature and umbilical or epigastric in site, but, with the onset of local peritonitis in the hernial sac, there may be a shifting of the pain to the appendicular region. Shock is often less in internal hernial strangulation owing to the tightness of the orifice often being less than in external hernia, with less violent constriction of the mesentery.

The diagnosis of a strangulated internal hernia is thus only likely to be made by exclusion of obvious causes of small-gut obstruction, such as external herniæ, post-inflammatory adhesions, etc.; the presence of a high intestinal obstruction in association with a tender, resonant mass, probably with slight muscular guarding, occurring in one of the recognized sites for the retroperitoneal fossæ, should suggest the possibility of an internal hernia.

The results of 26 cases of paracæcal hernia with strangulation (including the present case) show that there is considerable delay in the commencement of treatment and a resulting high mortality-rate :—

RESULTS IN 26 CASES OF STRANGULATED PARACÆCAL HERNIA.*

Operated upon	20
Recoveries after operation	14
Deaths after operation	5
Deaths without operation	6
Uncertain result	1
Mortality after operation	18·5 per cent
Longest duration of symptoms	21 days
Shortest duration of symptoms	24 hours
Average duration of symptoms	5·4 days
Average duration of symptoms in fatal cases.. ..	5·1 days
Cases requiring resection	4
Deaths after resection	1
Recovery after resection	3

* These figures include only those of which I could obtain more or less detailed records.

Rendle Short[13] in 1925, reviewing the literature, found a mortality of 23·5 per cent in retrocolic herniæ and 20 per cent in the ileo-appendicular variety, the average being thus 21·7 per cent in these types.

DOUBLE INTESTINAL OBSTRUCTION

Finsterer collected 44 cases of double acute intestinal obstruction from the literature and reported a case of his own of simultaneous strangulation in a properitoneal inguinal hernia and in the retrocolic fossa. A brief summary of this case is appended :—

Finsterer's Case.—A male, aged 33, noticed an inguinal hernia for four months. He was admitted with four days' history of acute intestinal obstruction with signs of strangulation of this hernia. Spontaneous reduction of the hernia occurred with relief of symptoms. Twenty-four hours later there was a recurrence of symptoms and the hernia was again strangulated. Laparotomy through a right pararectal incision revealed a large proporitoneal hernia near the right internal abdominal ring, with a diverticulum extending along the inguinal canal. After division of the sac 10 cm. of bowel were liberated, but the intestine was still anchored by its distal end. Further exploration showed the distal ileum to be strangulated in a retrocolic hernia. This portion was freed and 1·5 cm. were resected; continuity was established by end-to-side anastomosis with the cæcum. The patient recovered.

Finsterer classifies cases of double intestinal obstruction into two groups :—

1. **Primary Chronic Intestinal Obstruction** followed by a resultant hernial strangulation precipitated by the chronic intestinal distension (" Kombination Ileus " of von Hochenegg).

2. **Double Acute Obstruction.**—This includes double external hernial strangulation, external plus internal hernial strangulation, hernia plus volvulus, etc.

The mortality of these cases of double intestinal obstruction in 75 per cent owing to the overlooking of the second obstruction. The anal-ward obstruction is always primary, and, if situated in an external hernia, the higher lesion is likely to be missed; Finsterer therefore advises that in all cases the distal loop should be carefully examined as well as the proximal. If the distal loop is dilated, the inference that there is a lower obstruction is obvious, and this should be sought. The proximal loop should be drawn well down, if it appears to be tethered, and the cause of this should be investigated, as this tethering may be the only indication of a higher obstruction due to an internal hernia.

The case of internal hernia through the foramen of Winslow reported in this paper belongs to the first group of " Kombination Ileus." The danger would appear to be less than in Finsterer's second group, as the hernial strangulation is the more prominent feature, and, in external herniæ, the distension of the distal loop would be more obvious and would lead to investigation. A real danger would, however, arise in a case such as I have described if the operation of blind cæcostomy were contemplated in view of the gross cæcal distension. I have seen a case in a woman of 60 presenting similar features of acute intestinal obstruction with ballooning of the cæcum. A blind cæcostomy was performed under local anæsthesia but failed to relieve her pain or vomiting. At autopsy a carcinoma of the transverse colon was found to be causing obstruction, but the terminal event was an acute jejunal obstruction due to kinking by adhesion to the growth.

It appears, therefore, to be essential to be aware of the possibility of double intestinal obstruction in every case, and if circumstances have prevented thorough examination at the time of operation, any unexpected interruption in the immediate post-operative course should lead to a rapid investigation to

eliminate this factor. The necessity for adequate exposure and examination of both loops in all hernial strangulations, and for laparotomy rather than blind enterostomy in all suitable cases of intra-abdominal intestinal obstruction, has been admirably advocated by Finsterer to avoid the appalling mortality of this rather uncommon catastrophe.

CASES OF PARACÆCAL HERNIA REPORTED SINCE 1925

Moynihan collected records of cases up to 1906, and Rendle Short revised the literature up to January, 1925. The following cases have been collected from 1925 to 1934 :—

Hernia into the Ileo-appendicular Fossa.—

1. MALCOMB[14] (1927).—Male, aged 18. Symptoms of acute obstruction; similar attack three years previously. Diagnosis: Appendicitis. Operation: Reduction—recovery.

2. STITCH[15] (1927).—Age and sex ? Case of strangulation of 2 metres of the ileum in cavity above the cæcum opening by an orifice between the appendix and terminal ileum. Donald, who quotes this case, regards it as an anomalous fossa similar to that in his case (q.v.).

3. TRAUM[16] (1931).—Male, aged 64. Symptoms of acute obstruction. Diagnosis: Acute appendicitis. Operation: Reduction—recovery.

Hernia into the Retrocolic Fossa.—

4. COLEY and HOGUET[10] (1929).—Male, aged 39. Symptoms of chronic abdominal pain for six months, no strangulation. Diagnosis: Retroperitoneal hernia (X-ray negative). Operation: Reduction—recovery.

5. HENNIG[17] (1926).—Female, aged 16. Acute abdominal pain for twenty-four hours; chronic abdominal pain for months previously. Diagnosis: Ovarian lesion. Operation: Resection of bowel—recovery.

6. VIDGOFF and STURGEON[18] (1930).—Age and sex? Symptoms of severe pain and vomiting for twenty-four hours. Diagnosis: Acute appendicitis or obstruction. Operation: Reduction—recovery. Cæcum formed part of hernial contents.

7. LONG[19] (1929).—Male, aged 24. Symptoms of colicky abdominal pain and nausea. Diagnosis: ? Operation: Reduction—recovery.

Hernia into the Fossa Iliaco-subfascialis.—

8. DUNN[6].—This case is mentioned in *Operations of Surgery* by Rowlands and Turner, but no record is available otherwise.

Hernia into Anomalous Openings.—

9. DONALD[20] (1930).—Male, aged 57. Symptoms of four days' central abdominal pain shifting to the right iliac fossa with fæcal vomiting. Diagnosis: Small-intestinal obstruction. Died two hours after operation. Autopsy: 16 in. of strangulated ileum in sac behind mesentery of terminal ileum and internal to the inner border of ascending colon; orifice behind the base of the appendix, which was itself fused with the anterior wall of the sac. Donald suggests that this sac was caused by failure of fusion of the parietal peritoneum with the primitive mesocolon during the terminal stage of development and rotation of the gut.

SUMMARY

1. A case of strangulated hernia into the fossa iliaco-subfascialis has been described in detail.

2. A case of double intestinal obstruction, due to a strangulated hernia through the foramen of Winslow superimposed upon colonic obstruction, has been described.

3. The anatomy and probable causation of the fossa iliaco-subfascialis has been discussed.

4. The symptomatology and diagnosis of paracæcal herniæ have been mentioned, and the results of cases described in the literature have been analysed.

5. The rare but important condition of double intestinal obstruction has been emphasized and the two types of this lesion have been briefly considered.

6. A summary of cases of paracæcal hernia described in the literature since Rendle Short's revision in 1925 has been included.

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THE VALUE OF THE UREA-CLEARANCE TEST IN URINARY SURGERY*

By E. W. RICHES

ASSISTANT SURGEON AND ASSISTANT UROLOGIST TO THE MIDDLESEX HOSPITAL,

AND J. DOUGLAS ROBERTSON

CLINICAL CHEMICAL PATHOLOGIST TO THE MIDDLESEX HOSPITAL

THE determination of the renal function in nephritis has received a great deal of attention from workers in all countries, but less attention seems to have been paid to the renal element in urological surgery. The degree of renal function impairment consequent upon prostatic obstruction plays a large part in the immediate risk of prostatectomy. Cohen, Dodds, and Webb[1] drew attention to the necessity of assessing the renal function in operations on the prostate, and suggested the determination of the non-protein nitrogen of the blood. Dukes,[2] as recently as 1934, claimed that the blood-urea was of more value than any other single test in surgical disease of the urinary tract. Van Slyke and his collaborators[3] have, however, shown that the urea-clearance test possesses many advantages over other tests of renal function, so it was decided to employ this test in the present investigation.

Comparison of the urea-clearance test with other tests generally employed may be summarized thus :—

Blood-urea.—Van Slyke has pointed out the disadvantages of employing this figure alone. Further, Mackay and Mackay[4] have shown that the blood-urea does not begin to rise until the kidneys are reduced to half their original functioning power. As a means of assessing renal damage the blood-urea may be said to be of little clinical value, as it depends in part on the protein intake.

Urea-concentration Test.—McLean and De Wesselow[5] drew attention to this test, and it held many advantages over isolated blood-urea determinations. It consisted in collecting specimens of urine every hour for three hours, after a dose of 15 grm. of urea by mouth. The kidneys are considered efficient if urea rises above 2 per cent in any specimen. The objections to this test are the dependence of the result on absorption from the gut and the fact that it is possible to have a high concentration of urinary urea with severe renal impairment, i.e., a very high blood-urea.

Blood-creatinine.—The blood-creatinine has been considered a very good index of renal function, and Holten and Rehberg[6, 7] have discovered a ratio obtained from the rate of creatinine excretion after a dose by mouth. They report good results, but the method of determination of blood-creatinine is a colorimetric one which produces a great error.

Phenolsulphonephthalein.—It has been shown by careful work by Van Slyke that the urea-clearance registers fall in renal function some weeks or months before the phthalein excretion does.

It can be seen that the urea-clearance possesses many advantages over other tests. It is a more delicate indicator of fall in function than the others, and in addition it does not depend upon the excretion of a foreign substance. The kidney is observed working under normal physiological conditions.

EXPERIMENTAL

The cases studied consisted of: (1) Prostatic obstruction; (2) Renal tuberculosis; (3) Renal and ureteric calculi; (4) Hydro- and pyonephrosis; (5) Miscellaneous group.

Technique of Test.—The examination was performed in the morning after breakfast or in the afternoon after lunch. No preparation of the patient was carried out, except that no coffee was taken with the previous meal. The patient was at rest on a chair or couch during the test because exercise had been found to influence the results. Blood was withdrawn a few minutes before the end of the first hour. Patients were instructed not to void urine within three hours of their attendance, because of the uncertainty of emptying the bladder completely when containing only a small amount of urine. During the test the same difficulty of voiding urine was experienced at the end of the hour. This could be partially overcome by giving the patient a glass of water at the beginning and again at the end of the first hour. It was found that if a greater amount than this were drunk, while urination was made easier, there was a tendency to produce too low a urinary urea for accurate determination. It is most important that accurate time intervals be kept, and a stop-watch was employed to ensure accuracy to within a quarter of a minute. The duration of the period need not be one hour; it may be forty-five minutes, provided always the exact time is noted. It has been calculated that an error of one minute in the time interval produces an error of 1 per cent in the final renal function estimate. Another source of error is incomplete emptying of the bladder. It has been our custom to catheterize all women and all prostate cases. An example is shown demonstrating the accuracy of the test when carried out as described above :—

H. J., aged 49. Diagnosis: Carcinoma of kidney.

> 10–10.02 a.m.—Catheterized and bladder emptied. Specimen discarded.
> 10.55.—Bled of 5 c.c. of blood.
> 11.02.—Bladder emptied by catheter (Specimen 1).
> 12.02.—Bladder emptied by catheter (Specimen 2).
> Blood-urea = 30 mgrm. per 100 c.c.

1st Hour.—Urinary-urea = 0·4 grm. per cent = 400 mgrm.
> Urine volume = 160 c.c. per hour (2·66 c.c. per minute).

$$\text{Maximum Clearance } (C_m) = \frac{U}{B} \times V$$

$$= \frac{400}{30} \times 2 \cdot 66 = 35 \cdot 5 \text{ c.c.}$$

Normal is 74 c.c.

$$\therefore \text{ Percentage of normal} = \frac{35 \cdot 5}{74} \times 100 = 47 \text{ per cent of normal.}$$

2nd Hour.—Urinary urea = 0·6 grm. per cent = 600 mgrm. per cent.
Urine volume = 92 c.c. per hour (1·53 c.c. per minute).

$$\text{Standard Clearance } (C_s) = \frac{U}{B} \times \sqrt{V}$$

$$\approx \frac{600}{30} \times \sqrt{1\cdot53}$$

$$\approx \frac{600}{30} \times 1\cdot24 = 24\cdot0 \text{ c.c.}$$

Normal is 54 c.c.

$$\therefore \text{ Percentage of normal} = \frac{24}{54} \times 100 = 44 \text{ per cent of normal.}$$

Mean = 45·5 per cent.

This patient's renal function was only 46 per cent of normal. During the present investigations, results which did not agree within 10 per cent were repeated.

PROSTATIC OBSTRUCTION

From the surgical point of view the importance of having available a reliable test of renal function in cases of prostatic obstruction cannot be overestimated. In this condition any impairment of function is likely to involve the two kidneys equally, and it was therefore hoped that the urea-clearance test might prove of especial value in this connection ; it may be stated at the outset that in our opinion this hope has been realized.

Summary of Results.—The test has been successfully carried out upon 70 patients suffering from prostatic obstruction. Of these, 58 have subsequently undergone operative treatment upon the prostate, either by endoscopic resection or suprapubic prostatectomy, and in the latter group the Harris operation has been performed in the more recent cases. The remaining 12 include cases treated by medical means and dilatation and those still undergoing drainage with a view to increasing their renal function, and they are analysed separately.

(Throughout this section the term ' two-stage ' is used for cases in which preliminary suprapubic drainage was carried out; cases in which an indwelling catheter was sufficient are classed as ' one-stage ' operations.)

Table I sets out the total number of cases treated by each method, with the operative deaths.

Table I.—All Cases Operated Upon

OPERATION	NUMBER	DEATHS
One-stage prostatectomy	21	3
Two-stage prostatectomy	2	1
One-stage endoscopic resection ..	29	1
Two-stage endoscopic resection ..	6	1
Total ..	58	6

The cases treated by resection include 10 cases of prostatic carcinoma.

Table II includes all cases in which the urea-clearance test showed a renal function of not less than 60 per cent at the time of operation.

Table II.—FUNCTION ABOVE 60 PER CENT

OPERATION	No	WELL	DIED	CAUSE OF DEATH
One-stage prostatectomy ..	19	17	2	1 Heart failure* 1 Pulmonary embolism
Two-stage prostatectomy ..	1	1	–	
One-stage endoscopic resection	24	24	–	
Two-stage endoscopic resection	5	5	–	
Total ..	49	47	2	

* This patient died fifteen minutes after leaving the theatre, no post-mortem was obtained

Table III includes all cases in which the urea-clearance test showed a renal function of less than 60 per cent at the time of operation.

Table III.—FUNCTION BELOW 60 PER CENT

OPERATION	No	FUNCTION	WELL	DIED	CAUSE OF DEATH
		Per cent			
One-stage prostatectomy ..	2	52	1	–	
		59	–	1	Prolonged suprapubic fistula, bronchopneumonia
Two-stage prostatectomy ..	1	52	–	1	Uræmia
One-stage endoscopic resection	5	50	1	–	
		55	–	1	Uræmia — sepsis*
		59	1	–	
		55	1	–	
		57	1	–	
Two-stage endoscopic resection	1	48	–	1	Uræmia
Total	9		5	4	

* A case of carcinoma of the prostate with infected hydronephrotic kidneys

Table IV shows the cases not operated upon. The reasons for not operating upon these patients included poor renal function, insufficient symptoms, and the presence of intercurrent disease.

Table IV.—CASES NOT OPERATED UPON

TREATMENT	NUMBER
Suprapubic drainage ..	6
Medical and dilatation	4
Refused treatment .. .	2
Total ..	12

Of the cases drained, two died, one (function 30 per cent) from uræmia, and one (function 85 per cent) from pelvic abscess. Of the remainder, three will

probably come to operation, as their renal function improves, although it has in this series been found that a urea-clearance of 60 per cent is less easily attained after suprapubic drainage than by catheter drainage. This may be due to the fact that the cases submitted to suprapubic drainage are initially in worse condition than the others.

Comparison with other Renal Function Tests.—In all of these cases a comparison is possible between the renal function as estimated by the urea-clearance test and that determined by an estimation of the blood-urea, as a measurement of the latter forms part of the urea-clearance test. In some, various other tests have been performed, such as the urea-concentration test, indigo-carmine test, and a renal X-ray after uroselectan. A few cases may be quoted from the series to illustrate the fallacies of some of the other tests, and in particular the false security into which a blood urea determination may lead one.
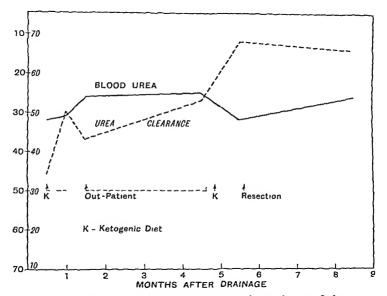
FIG. 86.—*Case* 1 Chart showing blood-urea and urea-clearance findings

Case 1 (*Fig.* 86).—A. W., aged 58, admitted with acute retention of urine due to a fibrous prostate. The urine was heavily infected and the general condition poor.
The clinical condition showed the need of drainage, and suprapubic cystotomy was done. After a fortnight the blood-urea was 32 mgrm. per cent, but the urea-clearance only 34 per cent. X-rays after uroselectan showed poor secretion from both kidneys with some dilatation of the pelves. A fortnight later with a ketogenic diet for part of the time the urea-clearance rose to 50 per cent, the blood-urea being 31 per cent. The ketogenic diet was withheld for the next fortnight, when the urea-clearance had fallen to 43 per cent, with an improvement of blood-urea to 26 mgrm. per cent   The patient was then discharged from hospital and treated as an out-patient for a further three months, by which time the urea-clearance had risen to 53 per cent, whilst the blood-urea remained fairly constant at 25 mgrm. per cent. He was then re-admitted and given a partial ketogenic diet, and one month later the urea-clearance had risen to 68 per cent, whilst the blood-urea had deteriorated to 32 mgrm. per cent. At this stage endoscopic resection of the prostate was performed and he made an uninterrupted recovery, the suprapubic wound being dry on the eleventh post-operative day. Three months after operation the urea-clearance was 66 per cent and the blood-urea 26 mgrm.

per cent. He now, more than a year after the operation, has no urinary symptoms, no infection, and there is no residual urine.

It is unlikely that this result would have been achieved without prolonged drainage, the necessity for which was only shown by the urea-clearance figures. The blood-urea figures were definitely misleading. The uroselectan pictures also indicated considerable renal damage but did not give an accurate idea of its severity ; in another case with a urea-clearance of only 59 per cent uroselectan was excreted in good concentration on both sides, the only abnormality shown being slight dilatation of the pelvis and ureter on the left side. Whilst excretion urography gives a visible indication of renal impairment, it is not sufficiently exact to be used as an index of operability in cases of prostatic obstruction.

Case 2.—E. C. M., aged 68, a diabetic, with prostatic symptoms and more than one pint of residual urine, due to a glandular enlargement of the prostate. The blood-urea was 49 mgrm. per cent ; the urea clearance-test was unsatisfactory as the two specimens at intervals of an hour did not agree within 10 per cent.   Intravenous indigo-carmine was excreted faintly from each kidney after twenty minutes. Drainage by indwelling catheter was instituted, and after five days indigo-carmine was excreted in poor concentration after eleven minutes. After eight days the urea-clearance was 111 per cent, blood-urea 31 mgrm. per cent, and indigo-carmine was excreted in good concentration at ten minutes.   Suprapubic prostatectomy by the Harris technique was performed on the tenth day, and progress was uneventful. The suprapubic wound remained dry, and urine was passed naturally when the urethral catheter was removed on the tenth post-operative day.

In this case the indigo-carmine test gave a reliable indication of renal function, but it is not so accurate as the urea-clearance ; the estimation of depth of colour is not easy unless a standard is available for comparison. The test, however, has the advantage of being easily carried out at the bedside and of being interpreted immediately. It therefore forms a useful check during the period of drainage to indicate when another clearance test should be performed.

Case 3.—E. P., aged 70, admitted with symptoms due to a glandular enlargement of the prostate. Drainage by indwelling catheter was instituted and tests of renal function were carried out. The blood-urea was 56 mgrm. per cent, urea-clearance 30 per cent, and the urea-concentration test showed 1·3 per cent in the first specimen, 1·4 per cent after one hour, and 1·9 per cent after two hours.   In view of the unsatisfactory results of these tests, suprapubic cystotomy was performed, but the patient gradually went into uræmia and died three days afterwards in coma.

In this case all three tests showed a serious impairment of renal function, but the urea-clearance test gave the most certain indication of the extremely grave prognosis.

The urea-concentration test is undoubtedly of value in these cases, but apart from the fallacies which have already been pointed out it suffers from others ; for example, it is interpreted differently by different observers, and whilst some would consider a high initial urea value essential for good function, others would look on a high range of increase as of more importance.

Effect of Drainage.—It has been pointed out that infection plays a large part in depressing renal function, and drainage alone, whether by suprapubic tube or indwelling catheter, will do little to combat infection and may even increase it unless other measures are applied to overcome it. The lowest value for the urea-clearance in this group was 29 per cent ; this patient (G. C.), whose urine was infected, was sent out after suprapubic cystotomy, and after fourteen months'

drainage and treatment as an out-patient his function is only 49 per cent. In another case (R. E.), admitted with a suprapubic cystotomy done elsewhere some months previously for prostatic carcinoma, the function on admission was 42 per cent, the urine being infected. After eleven days' in-patient treatment on forced fluids, urinary antiseptics and frequent lavage, the function had risen to 64 per cent, and it was then possible to carry out endoscopic resection; the fistula closed and he was restored to urinary comfort.

The greatest increase after drainage was 56 per cent; in this patient (J. H.), who had over a pint of residual urine and a large glandular prostate, the urea-clearance on admission was only 35 per cent and the urine not infected. After six days' drainage by indwelling catheter it had risen to 91 per cent and a one-stage prostatectomy was performed. Drainage by a urethral catheter appears to be particularly effective in restoring impaired renal function in cases where there is no urinary infection; adequate steps must be taken to prevent the ingress of infection via the catheter, and we now employ a modified Duke's apparatus as a routine for all cases in which an indwelling catheter is necessary for any purpose, so that frequent antiseptic irrigations can be easily carried out. Drainage by suprapubic cystotomy was necessary in only 7 cases out of the 52 who have undergone operations on the prostate, although it is still proceeding in four others, and two died after drainage alone (see Table IV).

The Safety Level of Renal Function in Prostatic Cases.—It is necessary to have some standard value of renal function below which operations on the prostate itself, apart from drainage operations only, should not be undertaken, and above which such operations may be safely undertaken, due consideration being given to other factors in the clinical condition of the patient which might influence the result. After a short experience of the test, the figure of 60 per cent was taken arbitrarily as the lower limit of safety. If the urea-clearance test shows a renal function of less than 60 per cent, no operation is undertaken on the prostate until the function has been raised to this figure by catheter or suprapubic drainage. The figure chosen is possibly rather too high, and in the absence of other complications 55 per cent would probably give an adequate margin of safety. At the same time it may be stated that no deaths from uræmia have occurred after prostatic operations where the function reached 60 per cent, whilst there were three deaths in which uræmia played the most important part in cases where the pre-operative renal function was less than 60 per cent. In some cases of death after prostatectomy it is impossible to assess the relative importance of uræmia and infection as causes of the fatal issue; the two factors appear to be intimately connected, for an infected kidney is more likely to fail and a damaged kidney is more easily infected. The urea-clearance test appears to bear this out, as it has been noticed that those cases in which there is urinary infection tend to have a lower renal function than the non-infected cases. It has also been noticed that cases that were operated upon when the renal function was very near 60 per cent have tended to have a more stormy and prolonged convalescence than those with a higher figure.

Some criticism of our interpretation of these results may be made on the grounds that many of the patients were treated by endoscopic resection, a procedure which carries less risk than prostatectomy. It is, however, quite certain that an adequate renal function is just as necessary for the one operation as the other;

one case treated in the days before we used the urea-clearance test as the criterion of operability illustrates this point forcibly :—

E. G. H., aged 88, had lived a catheter life for two years on account of prostatic enlargement, and catheterization was becoming increasingly difficult; there was residual urine amounting to 14 oz. and the blood-urea was 57 mgrm. per cent. After six weeks' suprapubic drainage, the blood-urea had fallen to 43 mgrm. per cent; this was considered a safe level, and endoscopic resection was carried out without difficulty. After operation he secreted no urine, and within fourteen hours was in coma. Thirty-one hours after operation he died. This death was purely uræmic, and had we been using the urea-clearance at that time, he would probably never have been operated upon.

To summarize the results in cases of prostatic obstruction we would state that, whilst the clinical condition of the patient is the ultimate deciding factor in assessing the operability, assistance from laboratory tests is necessary to tell us when the renal function is sufficiently good to allow an operation on the prostate to be carried out in safety. Of the tests used, we have found the urea-clearance test to be the most reliable ; the urea-concentration test has not given such accurate information in the borderline cases ; estimation of the blood-urea only shows extreme degrees of renal impairment, and may be misleading ; excretion urography demands such standardization of X-ray technique as to make it unsuitable for general application ; excretion of indigo-carmine is a useful bedside test, but its interpretation is not sufficiently accurate for borderline cases.

The insistence on a urea-clearance of 60 per cent may result in the withholding of the benefits of operation from a small number of cases, but it is undoubtedly a potent factor of safety for the majority. The adoption of this standard has already effected a considerable lowering of the mortality of operations on the prostate in this hospital.

At the beginning and throughout the investigation, the urea-clearance test was carried out in a number of surgical renal conditions. It was found after a time that whilst the results were of considerable interest, they were not of such value to the surgeon as in the prostatic cases ; in consequence the test was not adopted as a routine, and hence the number of cases in each group is relatively small. In several cases where the urea-clearance was low, the test has been repeated at intervals after the operation, and in this way some facts of importance in prognosis have been brought to light.

The conditions investigated are classified into the following groups : (1) Renal tuberculosis ; (2) Renal or ureteric calculus ; (3) Hydronephrosis and pyonephrosis ; (4) Miscellaneous affections of the kidneys and bladder.

RENAL TUBERCULOSIS

Twelve patients with proved renal tuberculosis have been investigated before operation, and in addition four patients who had undergone nephrectomy for this condition at varying intervals before, have been tested. *Table V* gives the details of the cases investigated pre-operatively ; as well as the urea-clearance it includes the blood-urea figures, the presence or absence of secondary infection of the urine, the findings on excretion urography with either uroselectan or abrodil, an estimate of the degree of kidney damage found at operation, and notes on the subsequent progress of the case. The cases are arranged in the order of their urea-clearance values, starting with the lowest.

Table V.—Renal Tuberculosis

PATIENT	SEX AND AGE	UREA-CLEARANCE	BLOOD-UREA	S.I.*	EXCRETION UROGRAPHY	KIDNEY DAMAGE FOUND AT OPERATION	PROGRESS
		Per cent					
1. L. D.	M. 14	18	54	o	Dilatation of both pelves	No operation (Bilateral)	Died 1 year later
2. L. P.	F. 23	33	27	o	Calcification. Normal pelvis	Moderate	Clearance rose to 103 per cent after 8 months. Well 18 months later
3. E. F.	F. 23	35	32	o	Filling defect	Extensive	Clearance fell to 32 per cent. Well 12 months later
4. H. D.	F. 29	56	30	o	Dilatation of pelvis	Extensive	Well
5. E. P.	F. 34	56	30	o	Poor concentration	Moderate in upper half of double kidney Lower normal	Well
6. W. C.	M. 55	57	26	o	Poor concentration. Other kidney enlarged	Extensive	Bilateral infection. Died of uræmia 13 months later
7 R. N.	F. 16	60	37	o	No excretion on affected side	Moderate	Clearance rose to 83 per cent after 8 months. Well 27 months later
8. J. P.	F. 28	70	29	B. coli	Filling defect	Moderate	Well 20 months later. Clearance fell
9. E. D.	F. 31	70	22	o	Dilatation. Calcification	Slight	Clearance rose to 98 per cent after 1 month. Well
10. J. G.	M. 45	100	28	o	Dilatation of ureter	Slight	Well 12 months later
11. L. C.	M. 30	100	25	o	Filling defect	Slight	To sanatorium for pulmonary infection
12. A. B.	M. 23	120	24	o	No excretion on affected side	Slight	Well 5 months later

* S.I. = Secondary infection.

It will be seen that the lowest urea-clearance in the series was 18 per cent; this was in a boy with extensive bilateral involvement on whom no operation was performed and who died subsequently. In one other case (*Case* 6) bilateral infection was suspected, and it became manifest within a year of nephrectomy; the urea-clearance in this case was 57 per cent and the patient died of uræmia thirteen months after operation. All the other patients are known to be alive and well.

The lowest urea-clearance at which nephrectomy was successfully performed was 33 per cent (*Case* 2), and in this case it rose to 103 per cent eight months after operation, a fact which was in full agreement with the satisfactory clinical condition. *Cases* 7 and 9 also showed a considerable rise in function after the offending kidney had been removed. In two cases there was a fall in the urea-clearance value after operation. In *Case* 3 the figure was 35 per cent before operation and 32 per cent six months later, but whilst originally there was no secondary infection, on the second occasion there was a definite *B. coli* infection of the urine. The other case in which there was a diminution in the urea-clearance value after operation (*Case* 8)

had a secondary *B. coli* infection at the time of operation ; in her case the test was repeated at intervals for a year with the following results :—

INTERVAL			UREA-CLEARANCE Per cent		BLOOD-UREA Mgrm. per cent
Pre-operative	..	..	70	..	29
1 months ..	..	..	70	..	24
3 months ..	..	..	35	..	31
12 months ..	..	..	63	..	21

It seems fair to presume that the secondary infection was the deciding factor in preventing the rise in function after the removal of a diseased kidney which the other cases led us to anticipate.

The blood-urea figures show that only in the case where the urea-clearance was only 18 per cent was the blood-urea raised above what is commonly accepted as normal ; an isolated estimation of the blood-urea appears to be of value only in the extremes of renal dysfunction.

Excretion urography was frequently of considerable help in confirming which was the affected side, but gave no clear idea of the amount of renal damage.   If the ureter is blocked from any cause, it would appear that there may be no excretion of the dye on that side ; this occurred in two cases (*Cases* 7 and 12), in which at operation only moderate or slight renal damage was found, but in which the X-ray picture was identical with that obtained in complete destruction of all the secreting tissue.

The extent of the destruction of the kidney substance found at operation is classified as extensive, moderate, or slight, and it will be seen that this degree of damage is forecast more closely by the urea-clearance test than by any other of the tests employed.

The indigo-carmine test was performed in some cases, but with this also there was no indication of the degree of destruction in the moderately damaged cases.

From the surgical point of view, the most important conclusion to be drawn is that when the infection is confined to one kidney nephrectomy is usually safe whatever the total renal function may be ; provided that there is no secondary infection, the function as estimated by the urea-clearance test will probably show an improvement after removal of the diseased kidney.

Table VI shows the results of the test in four cases investigated at varying intervals after nephrectomy for tuberculosis ; in each case the patient is alive at present and apparently well.

Table VI.—RESULTS AFTER NEPHRECTOMY

INTERVAL AFTER NEPHRECTOMY					UREA-CLEARANCE
					Per cent
14 months	..	..	..	..	70
5 years	..	..	..	..	40
5 years	..	..	..	..	43
10 years	..	..	..	..	62

RENAL AND URETERIC CALCULI

The test was performed in 10 cases of stone in the upper urinary tract ; of these, 6 were unilateral and 4 bilateral.   The results are given in *Table VII* together with the relevant clinical data.

Table VII.—RENAL AND URETERIC CALCULI

PATIENT AND AGE*	SITE	UREA-CLEARANCE	BLOOD-UREA	S.I.†	EXCRETION UROGRAPHY	PROGRESS AFTER OPERATION
Unilateral.—		Per cent				
1. J. G. 59	U.	62	55	*B. coli*	Normal	Diabetic. Well
2. L. R. 38	U.	80	39	o	Slight hydroneph-nephrosis	Well
3. S. D. 38	U.	80	28	o	Slight hydroneph-rosis	Clearance rose to 98 per cent after 1 month
4. A. R. 52	U.	80	30	o	—	Tested 4 years after passing stone
5. S. J. 43	K. Pelvis	90	31	o	—	Well 3 years later
6. C. S. 34	U.	100	27	o	—	Well 18 months later
Bilateral.—						
7. E. H. 29	K. Pelvis	56	34	o	—	Multiple calculi
8. H.B. 52	K. and U.	62	26	o	L., slight hydro-nephrosis ; R. considerable hy-dronephrosis	L. renal and ureteric R. multiple stones and papillary adenocarci-noma
9. A. H. 38	K. Pelvis	65	36	*Staph.*	Bilateral hydro-nephrosis	Extensive renal damage
10. M. A. 49	K. Pelvis	82	42	*B. coli*	R. hydronephrosis	Fairly well. No operation

* All these cases were males, and all were treated surgically except *Cases* 4 and 10.
U = Ureter ; K = Kidney.   † S.I. = Secondary infection.

In the cases of unilateral calculi the urea-clearance was 80 per cent or more in all but one, and this was the only case with infection. Improvement after removal of the stone was recorded in the only case in which the test was repeated.

In the bilateral cases the clearance was below 66 per cent in all but one ; this patient has a surprisingly good renal function. He has a history of stone extending back for twenty-five years, and there are now multiple branching calculi in the right kidney and a single one in the left. Both kidneys concentrate uroselectan fairly well, although the right is hydronephrotic ; indigo-carmine is excreted from the right side in four and a half minutes, and from the left in four minutes, in keeping with a urea-clearance of 82 per cent. The patient declined to consider operation and has been treated for four years by urinary antiseptics and bladder lavage.

HYDRONEPHROSIS AND PYONEPHROSIS

This group includes six cases. *Table VIII* sets out the clinical and laboratory findings.

In this group again the fact that infection is a potent factor in lowering renal function is well illustrated. It is also made evident that where one kidney is completely atrophied, the total function may still be approximately normal, provided there is no infection. In *Case 4* the right kidney failed to secrete uroselectan and was found at operation to consist of a fibrous hydronephrotic shell with scarcely any renal substance, yet the clearance was 93 per cent. In *Case 5* there was very poor concentration of uroselectan, and no excretion of indigo-carmine after twenty minutes, yet the clearance was 100 per cent. After the removal of an infected kidney, or the correction of an obstructed ureter, the function tended to rise.

Table VIII.—HYDRONEPHROSIS AND PYONEPHROSIS

PATIENT	SEX AND AGE	CONDITION	UREA-CLEARANCE	BLOOD-UREA	S.I.*	TREATMENT	PROGRESS
1. E. C.	M. 36	R. pyonephrosis. Vessel crossing ureter	Per cent 35	37	+	Nephrectomy	Clearance rose to 50 per cent after 1 month, and 74 per cent after 10 months
2. R. R.	M. 34	R. hydronephrosis. Probably congenital	65	39	+	Plastic operation	Clearance rose to 74 per cent after 1 year
3. J. P.	M. 54	Stricture of urethra. R.pyonephrosis. L. hydronephrosis	75 after R. nephrostomy	28	+	R. nephrostomy. Dilatation of stricture	Eight months later L. pyonephrosis. Died of uræmia after L. nephrostomy
4. A. B.	M. 23	R. hydronephrosis	93	37	o	Nephrectomy	Complete destruction of renal tissue. Clearance 95 per cent after 4 months
5. L. P.	F. 40	R. hydronephrosis; L. slight dilatation	100	19	o	R. plastic operation	Indigo-carmine— L. 4 mins., R. o, (before operation)
6. D. D.	M. 36	L. hydronephrosis	100	22	o	Plastic operation	Well 6 months later

* S.I. = Secondary infection.

MISCELLANEOUS GROUP

The urea-clearance test was also carried out in a number of other surgical urological conditions which are shown in *Table IX*.

Table IX.—MISCELLANEOUS

PATIENT	SEX AND AGE	CONDITION	UREA-CLEARANCE	BLOOD-UREA	S.I.*	NOTES
1. H. J.	M. 49	Carcinoma of R. kidney	Per cent 46	30	+	Large tumour removed by abdominal nephrectomy. Clearance rose to 66 per cent after 1 month and 84 per cent after 5 months
2. F. S.	F. 58	Pyelitis	65	44	B. coli	—
3. B. S.	F. 58	R. pyelonephritis	70	40	+	Nephrectomy
4. F. M.	F. 47	Ureterocele	89	19	o	Removed by cystodiathermy
5. G. W.	M. 69	Carcinoma of bladder	100	30	Staph.	Growth did not involve ureter
6. W. E.	M. 65	L. renal tumour	100	27	o	Poor excretion of uroselectan. Refused operation
7. M. C.	M. 24	L. lumbar abscess	102	27	o	Pott's disease of spine. Kidney displaced by abscess

* S.I. = Secondary infection.

In *Case* 1 the depression of renal function was probably due to the infection, and its subsequent rise to the removal of the infected growth ; in *Case* 6 a non-infected growth showed a clearance of 100 per cent.

SUMMARY

1. The urea-clearance test is discussed, and the technique employed is described.
2. The results of the test in 109 surgical cases are tabulated.
3. The presence of urinary infection lowers the clearance value.
4. The test is reliable as an index of operability in prostatic obstruction; where the urea-clearance is over 60 per cent, operation is safe, whilst below this figure it is hazardous.
5. In unilateral lesions of the upper urinary tract, the total renal function is of little importance ; it improves after removal of the underlying cause, and a normal urea-clearance may be attained with only one kidney.

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THE EFFECT OF TRACHEAL OCCLUSION ON THE HYPERTROPHY OF THYROID TRANSPLANTS AND REMNANTS

By E. WALTER WORKMAN AND G. GAVIN MILLER

FROM THE DEPARTMENT OF EXPERIMENTAL SURGERY, MCGILL UNIVERSITY, MONTREAL, CANADA

INTRODUCTION

THE present work was carried out in order to study more closely the causes producing histological changes in the thyroid gland. The importance of iodine as a factor in producing thyroid gland changes was evident, but was not, apparently, the only factor. Breitner considered iodine was the controlling factor and that it tended to bring both the hyperactive and hypoactive gland back to the normal phase. In the present experiments identical changes were produced without directly interfering with iodine metabolism. Since this work was begun two years ago, the important work of Collip, demonstrating the presence of both thyreotropic and antithyreotropic hormones in the blood-stream, has been published. He has further demonstrated that these hormones maintain a balance, which he explains by his theory of "inverse response". To-day it would seem that bodily requirements for thyroxine upset the balance between thyreotropic and antithyreotropic hormones, thus increasing or decreasing the demand for thyroxine. Depending on the need for thyroxine the gland becomes hyperplastic, or goes into the resting phase. Iodine, as the most important constituent of thyroxine, has a definite place in this cycle. When one whole lobe of the thyroid gland and two-thirds of the other are removed from animals the remnant becomes hyperplastic. The remnant, having to do the work of the whole gland, is stimulated to activity, and hyperplasia results. Four or five months later, hypertrophy having resulted, stimulation stops and the gland again shows essentially normal structure histologically, though there may be traces of hyperplasia still remaining.

Breitner has shown that partial tracheostenosis produces a gland of low activity with increased colloid, the so-called resting phase.

Two simple mechanical means are consequently available to alter the histological picture of the thyroid at will—one, subtotal thyroidectomy, producing hyperplasia in the remnant; and the other, artificial tracheostenosis, producing a hypoactive gland.

The experiments to be described aim to produce, by means of partial tracheostenosis, a transition in the neck remnant left after subtotal thyroidectomy from the hypertrophic to the colloid phase; further to produce, if possible, identical changes in autotransplants. Breitner had not shown that tracheostenosis would produce the colloid phase in autotransplants as well as in the gland proper.

Such histological changes, if produced, suggest that the body requirements for thyroxine are altered by these experimental methods. If the autotransplants

showed identical changes, then it would follow that these changes must be due to a blood-borne factor—in other words, a hormone—and that this hormone was, to a certain extent at least, controlled by body requirements.

In this case the important position given to iodine in thyroid changes would need careful review. It could no longer be considered the controlling factor in thyroid function, but rather one in a chain of interrelated factors. Collip has since shown that such other factors do exist—namely, thyreotropic and antithyreotropic hormones.

HISTORICAL REVIEW

In 1919 Loeb[1] studied the structural changes in the thyroid gland of the guinea-pig after removal of from one-half lobe to more than one and two-thirds lobes of the gland. He concluded: (1) After removal of half of one lobe no definite changes occurred; (2) After removal of one lobe slight hypertrophic changes were noticed; (3) After removal of one and one-half lobes definite hypertrophic changes occurred; (4) After almost complete removal of both lobes marked changes were found in the remnants. These compensatory hypertrophic changes developed from the fifteenth to the eighteenth day after operation. Cell multiplication ceased from the twenty-second to the thirtieth day. Six to eight weeks after operation there was a new formation of colloid. There was still some evidence of hypertrophy four to five months after operation. The mitotic figures were most marked from the fifteenth to the seventeenth day after operation; subsequently they gradually decreased in number. He observed that hypertrophy was more marked when the animal gained weight,[1, 3] and during the colder months.[4, 6]

Loeb also showed that potassium iodide[4, 6, 8] intensified the compensatory hypertrophic changes, while thyroid, thyroxine, and anterior pituitary substance,[5-7] when given orally, had an inhibitory effect. The intraperitoneal injection of acid or alkaline extract of the anterior pituitary[9] into normal guinea-pigs produced a very intensive hypertrophy of the thyroid with a relative loss of weight. He suggested that this might be due to increased thyroid secretion discharged into the blood-stream, thus raising the metabolism.

In 1903 Cristiani[10] observed that compensatory hypertrophy occurred in thyroid autotransplants. In 1920 Loeb[2, 3] showed that the frequency, character, and degree of hypertrophy were similar in both remnants and autotransplants. Cristiani[11] concluded that structural changes in the transplanted glands were identical with those occurring in the thyroid of the host.

In 1912 Reich and Blauel[12] observed that, following partial tracheostenosis, the thyroid gland of the rat showed histological changes of a colloidal nature. These findings were confirmed by Breitner and Orator[13] in 1924. They studied the changes in gland structure in the rat following: (1) Removal of one lobe of the thyroid; (2) Tracheostenosis; (3) Tracheostenosis and removal of one lobe. They found that after removal of one lobe the other lobe became hyperactive; following tracheostenosis alone the gland became hypoactive; following removal of one lobe together with tracheostenosis, a balance appeared to be obtained and very little change was noted. The stimulation produced by extirpation of one lobe of the thyroid was apparently counterbalanced by the inhibiting effect of partial tracheostenosis. Breitner interpreted these changes as due to a storing up or flushing out of colloid in response to a demand for an increased or decreased metabolism from

the body. Breitner[14] then administered iodine to the rats after hemithyroidectomy and after partial tracheostenosis ; in the former the colloid did not disappear, while in the latter there was no increase of colloid. He considered that iodine had the power to inhibit the hyperactive gland and to stimulate the colloidal type. Since this was supported by clinical experience correlated with histological studies, Breitner concluded that iodine was the controlling factor in these histological changes, tending to keep the gland normal.

Carrari,[15] reporting the work of Silvagni in 1931, recorded that, following inhalation of asphyxiating gases, the thyroid gland showed an enlargement of the alveoli, flattening of the epithelium, and an increase in colloid.

Unknown to the authors, Abbott et al.[16] in 1933 repeated Breitner's work, using dogs, pups, and kittens. They showed that the thyroid in young animals is normally hyperplastic, and that tracheostenosis will cause a reversion of the hyperplastic gland to the colloidal type. They concluded that tracheal compression due to a large goitre played no part in the colloidal type of goitre found in these cases. Reich and Blauel, and Breitner, considered these colloidal changes were due to lack of oxygen. Abbott and his co-workers doubted this explanation and concluded that the problem was much more complex.

Collip and his co-workers have made important observations on the thyroid changes occurring in hypophysectomized rats after the injection of anterior pituitary extracts. In 1933 Anderson[17] showed that when an alkaline extract of anterior pituitary was injected into the rat only negligible changes were produced in the thyroid ; when the extract was injected together with *Staphylococcus aureus* vaccine a marked hyperplasia occurred with a coincident rise in metabolism. Loeb and Bassett,[9] Krogh,[18] and Baumann and Marine,[19] have all reported thyroid hypertrophic changes in dogs, rabbits, and guinea-pigs as a result of the injections of extracts of the anterior pituitary lobe.

Later in 1933 Anderson and Collip[20] isolated a purified extract of the anterior pituitary lobe containing the thyreotropic factor. Following hypophysectomy the rat thyroid shows marked colloid changes. This is transformed to the active cellular state by the injection of the purified thyreotropic extract. Coincident with this, Anderson and Collip[21] found a marked rise in the metabolic rate. In hypophysectomized rats the metabolic rate fell on an average to 74 per cent of the normal.

Further investigations by Collip and Anderson[22] demonstrated that when these injections are repeated over a prolonged period the metabolic rate again falls and cannot be increased by further injections or by transplanting normal thyroid glands. The serum of these rats was found to contain an antithyreotropic factor.

In March, 1934, Collip[23] explained these findings by his theory of " inverse response ". Normally there is a balance between the thyreotropic hormone and the antithyreotropic substance. In hypophysectomized rats the thyreotropic hormone is absent, while the antithyreotropic factor is diminished, as is evidenced by the increased sensitivity of the animal to the thyreotropic extract. The level of a hormone is apparently inversely proportioned to the level of its corresponding anti-hormones. Thus a hyperhormone state, associated with lowered response to injected hormones, implies the coexistence of a hyper-anti-hormone state.

Anderson and Collip[24] have not as yet found where the antithyreotropic substance originates, although they have isolated it from the blood serum.

Loeb and his co-workers[25] demonstrated that the acid extract of the anterior pituitary lobe induced an increase in the organic blood iodine at the expense of the organic iodine content of the thyroid gland. This was accompanied by a marked decrease in thyroid colloid. He concluded that the acid extract caused a diminution of the iodine of the thyroid.

METHODS

In the following experiments adult male and non-pregnant female guinea-pigs were used, since Loeb[1] has stated that these animals under normal conditions do not develop goitre. The previous work of Loeb and Breitner was first repeated in order to confirm their findings.

Ether anæsthesia was used throughout the experimental work. The skin was shaved and sterilized with mercurochrome. In all, 98 animals were used and 194 operations were performed. The partial ligature of the trachea in such a small animal always afforded some difficulty; when the ligature was drawn too tightly, the animal died in a few hours; if it was not tight enough, no changes occurred in the gland. In a few cases the ligature cut through the trachea, and a localized abscess developed. These animals were discarded. Attempts to pass a fine catheter down the trachea and to tie a ligature around it proved unsuccessful. Finally, the ligature was tied to a degree determined by experience. In every case the results of this method were verified by autopsy. The trachea was found to be stenosed to about one-quarter of its normal diameter in those cases which showed histological changes in the gland. Autotransplants, when used, were placed in the subcutaneous tissue of the abdominal wall.

Records of the weights of the animals were kept. The experiments were carried out during the colder months. A preliminary section was taken of each animal's thyroid gland as a histological control. Tissues were fixed in Zenker's solution immediately after extirpation. Paraffin sections were made and stained by the hæmotoxylin-eosin method

Throughout this work Loeb's[5] classification for estimating the degree of hypertrophy has been used. This classification depends on the shape of the acini, the type of cells, the amount of colloid, the presence of granules, and the appearance of mitotic figures. Loeb divides these changes into five gradations: Grade I, showing the greatest degree of hypertrophy, whilst Grade V shows normal structure (*Table I*).

The following criteria for the colloidal phase were adopted: (1) Acini were regular and generally larger than normal; (2) Acini cells were flattened or cuboidal; (3) Granules were indistinct; (4) Mitotic figures were absent; (5) The colloid was increased, filling the lumen of the alveoli.

It had been hoped to carry out metabolic rates, but the necessary apparatus was not available. Efforts were made to determine the oxygen tension of the blood before and after partial tracheal occlusion. An amount of blood sufficient to make these determinations by the usual methods could not be obtained from the guinea-pig; the apparatus for micro methods was not available. It had been hoped to study the hæmatological changes occurring during these experiments; although many hæmograms were studied, the results were so indefinite that this feature of the work was discontinued.

Table I.—LOEB'S CLASSIFICATION OF HYPERTROPHIC CHANGES IN
THYROID GLAND (MODIFIED)

	DEGREE	ACINI	CELLS	GRANULAR	COLLOID	MITOTIC FIGURES
Grade I ..	Highest	Irregular with papillæ	High columnar	Very distinct	Absent	Present
Grade II ..	Marked	Slit-like and irregular	High columnar	Distinct	Mostly absent Vacuolar	Present
Grade III ..	Decided	Somewhat irregular Some slits	Low columnar	Distinct	Diminished Vacuolar	Present
Grade III to IV ..	Moderate	Slightly irregular	Low columnar	Distinct	Soft, bluish Somewhat diminished	Present
Grade IV ..	Very moderate	Regular, occasionally irregular	Somewhat enlarged	Present	Some softening	Rare
Grade IV to V ..	Trace	Regular	Larger than normal	Indistinct	Solid with early vacuolization	Rare
Grade V ..	Normal	Regular	Flat to cuboidal	Indistinct	Solid Retracted	Very rare

EXPERIMENTS

EXPERIMENT I: *Production of Compensatory Hypertrophy following Extirpation of One and One-half to One and Three-quarter Lobes of the Thyroid Gland.*—Eleven guinea-pigs were used. Fifteen to nineteen days after the extirpation of from one
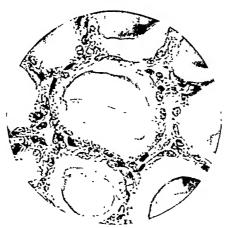
FIG. 87.—Normal thyroid gland of guinea-pig. Acini are regular. Epithelium lining the acini is low, cuboidal; some epithelial cells are flattened. Granules indistinct. Colloid is solid and retracted. (× 400.)

and one-half to one and three-quarter lobes of the thyroid gland, the remnants were removed and sectioned (*Fig.* 88), and were compared with sections taken at the first operation (*Fig.* 87). The remnants all showed varying degrees of hypertrophy, from a trace (Grade IV–V) to marked hypertrophy (Grade II). Six of the animals gained weight, three showed a moderate loss, and in two a slight loss was noted. In the higher grades of hypertrophy the acini were irregular, sometimes slit-like in form. In many acini papillæ were seen. The epithelial cells were high and wide with distinct granules and many mitotic figures; the colloid was softened, vacuolar, diminished, and in some absent; lymphocytes were increased.

FIG. 88.—Compensatory hypertrophy in neck remnant (Guinea-pig 38). Acini are irregular; some are converted into slits. Epithelial cells are high and wide. Granules are distinct. A mitotic figure may be seen in the section. Colloid is diminished and soft, while some of the alveoli contain no colloid. This section shows marked hypertrophy (Grade II). (× 400.)

EXPERIMENT II : *Compensatory Hypertrophy in Remants and Autotransplants.—* In seven guinea-pigs from one and two-thirds to one and three-quarter lobes of the thyroid gland were extirpated. One lobe was transplanted into the subcutaneous tissue of the abdominal wall; the remainder was sectioned to serve as a control. After fifteen to twenty-one days the animals were sacrificed. Three of the animals showed a gain in weight,
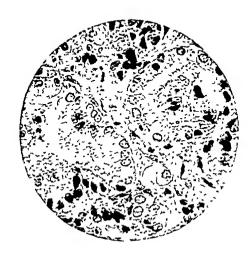
FIG. 89.—Compensatory hypertrophy in remnants and auto-transplants : neck remnant (Guinea-pig 84). Acini are irregular. Epithelial cells are high and wide; granules distinct. Colloid is markedly diminished and soft. Decided hypertrophy (Grade III). (× 400.)

FIG. 90.—Compensatory hypertrophy in remnants and auto-transplants: autotransplant (Guinea-pig 84). Some of the acini are irregular; some show slits. Epithelial cells are high and wide. Mitotic figures are seen in the section. Granules are distinct; colloid is markedly diminished and in some alveoli absent. Decided hypertrophy (Grade III). (× 400.)

while four showed a moderate loss.   In six of the animals the grades of hypertrophy in remnants and autotransplants were similar ; in one there was moderate hypertrophy (Grade III–IV) in the transplant but none in the remnant.   The hypertrophic changes in remnant and autotransplant are shown in *Figs.* 89, 90.   The acini are irregular, with papillæ.   The epithelial cells are high and wide, with distinct granules and many mitotic figures. The colloid is diminished to absent. Lymphocytes are increased.

EXPERIMENT III : *Colloidal Phase in the Thyroid as a Result of Partial Tracheostenosis.* — Four successful experiments were carried out.   A small portion of the normal thyroid was first removed as a histological control, the trachea was then partially stenosed by a silk ligature. When the animals were sacrificed ten to eleven days later, in all there was a stenosis of the trachea to about one-fourth of its normal diameter.   In three of the animals the body weight was constant, while one showed a marked loss.   The thyroid was then sectioned, and in each case the colloidal phase was noted (*Fig.* 91).   The acini were much larger than
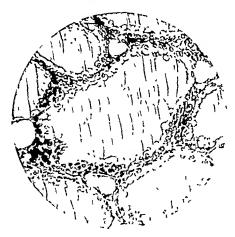
FIG 91 —Colloidal phase in neck remnant (Guinea-pig 15)   Acini are large   Epithelial cells are flattened , granules indistinct , no mitotic figures   Colloid fills the entire lumen. (× 90)

the normal, with flattening of the epithelial cells ; mitotic figures were absent, and the granules indistinct.   The alveoli were filled with colloid which, for the most part, took the eosin stain readily, although occasionally it assumed a light violet colour suggesting a new formation of colloid.

A number of guinea-pigs were used ; in some instances the animals died from asphyxiation due to tightness of the ligature ; in some examination at autopsy showed insufficient stenosis, so that gland changes had not occurred ; while in others there was cutting through of the ligature with infection.   All these animals were discarded.

EXPERIMENT IV : *Thyroid Changes following Simultaneous Tracheostenosis and Subtotal Thyroidectomy.*—In five guinea-pigs subtotal thyroidectomies and simultaneous tracheostenosis were carried out. After thirteen to eighteen days the animals were sacrificed.   In two instances there was a prominence of the colloidal phase, while in three there was hypertrophy (*Figs.* 92–94).   The weights were fairly constant ; one in which the colloidal phase predominated showed a gain of 147 grm.

FIG 92 —Simultaneous tracheostenosis and subtotal thyroidectomy (Guinea-pig 25)   Normal thyroid (control). (× 400)
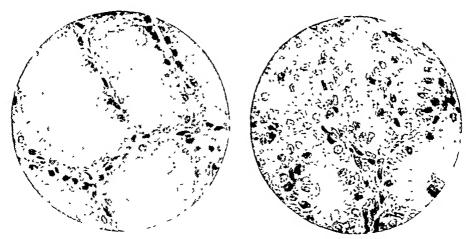
FIG. 93.—Simultaneous tracheostenosis and subtotal thyroidectomy. Neck remnant (Guinea-pig 25). Same animal as *Fig.* 92 after simultaneous tracheostenosis and subtotal thyroidectomy. Acini are large. Epithelial cells are flattened. Granules are indistinct ; no mitotic figures. Colloid fills the entire lumen ; it is, however, vacuolated.   (× 400.)

FIG. 94 —Simultaneous tracheostenosis and subtotal thyroidectomy. Neck remnant (Guinea-pig 68). Acini are irregular. Epithelial cells high and wide ; granules distinct ; mitotic figures present. Colloid is diminished and in some alveoli absent. Moderate grade of hypertrophy (Grade III–IV). (× 400.)

EXPERIMENT V : *The Effect of Partial Tracheostenosis on the Hypertrophic Remnants.*—Six successful experiments were carried out. One and one-half to one and three-quarter lobes of the thyroid were removed ; these served as histological controls. After fifteen to twenty-one days sections were taken from the remnant and partial tracheostenosis was instituted   These sections showed varying
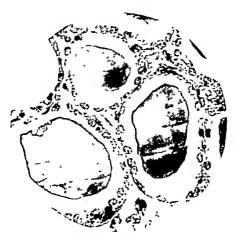
FIG. 95.—Effect of partial tracheostenosis on the hypertrophic neck remnant (Guinea-pig 52). Normal thyroid (control). (× 400.)

degrees of hypertrophy from a trace (Grade IV–V) to the highest degree (Grade I). Nine to thirteen days following tracheostenosis the animals were sacrificed ; all showed occlusion of the trachea to approximately one-quarter of its normal diameter. The thyroid gland remnants were sectioned. In three animals varying degrees of

reversion to the colloidal phase were observed (*Figs.* 95–97); in the other three hypertrophic changes had persisted. After the first operation there was little
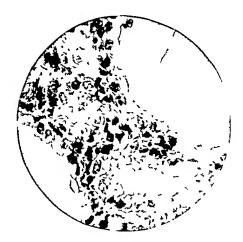
FIG 96 —Effect of partial tracheostenosis on the hypertrophic neck remnant (Guinea-pig 52) Some of the alveoli are wide, others are irregular Epithelial cells are higher than the normal In some they are high and wide, granules distinct Colloid diminished in some of the alveoli, in others it fills the lumen Very moderate hypertrophy (Grade IV) (× 400)

FIG 97 —Effect of partial tracheostenosis on the hypertrophic neck remnant (Guinea-pig 52) Acini are larger than the normal Epithelial cells are flattened Granules indistinct, no mitotic figures Colloid is solid and fills the entire lumen There has been a reversion to the colloidal phase Compare this with *Fig* 96 (× 400)

change in weight, except one which gained 133 grm. After the second operation all showed a small loss of weight, except one which gained 45 grm.

EXPERIMENT VI : *The Effect of Partial Tracheostenosis on Compensatory Hypertrophy of Thyroid Remnants and Autotransplants.*—In seven successful experiments
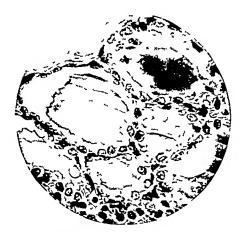
FIG 98 —The effect of partial tracheostenosis on compensatory hypertrophy of thyroid remnants and autotransplants (Guinea-pig 72) Normal thyroid (control) (× 400)

one and three-quarter lobes of the thyroid gland were excised. One lobe was transplanted into the subcutaneous tissue of the abdominal wall; the remaining

portion served as a histological control (*Fig.* 98). After fifteen to twenty-one days sections were made from the thyroid remnant of the neck (*Fig.* 99) and of the
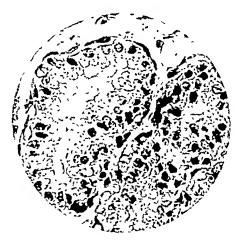
FIG. 99.—The effect of partial tracheostenosis on compensatory hypertrophy of thyroid remnants and autotransplants: neck remnant (Guinea-pig 72). Alveoli are irregular. Epithelial cells are high and wide. Granules distinct. A mitotic figure is seen in this plate. Colloid is markedly diminished, adherent, and vacuolated. Decided hypertrophy (Grade III). (× 400.)
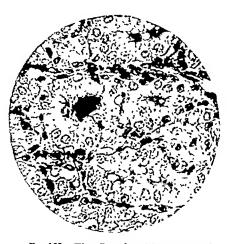
FIG. 100.—The effect of partial tracheostenosis on compensatory hypertrophy of thyroid remnants and autotransplants: autotransplant (Guinea-pig 72). Similar picture to that seen in the neck remnant (*Fig.* 99). Decided hypertrophy (Grade III). (× 400.)

FIG. 101.—The effect of partial tracheostenosis on compensatory hypertrophy of thyroid remnants and autotransplants: neck remnant (Guinea-pig 72). The alveoli are large; epithelial cells are flattened; a few are of cuboidal type. Granules indistinct. Colloid fills the entire lumen. This represents a reversion to the colloidal phase. Compare *Fig.* 99. (× 400.)
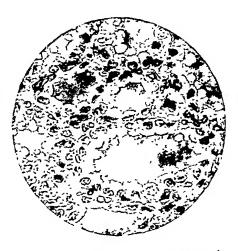
FIG. 102.—The effect of partial tracheostenosis on compensatory hypertrophy of thyroid remnants and autotransplants: autotransplant (Guinea-pig 72). Alveoli are large and regular. Epithelial cells are of the cuboidal type. Colloid fills the entire lumen. Reversion to the colloidal phase. Compare *Fig.* 100. (× 400.)

autotransplant (*Fig.* 100). These sections showed varying degrees of hypertrophy, from very moderate (Grade IV) to marked (Grade II). The animals showed no

marked change in weight. At this time partial tracheostenosis was instituted, and after ten to twelve days the animals were sacrificed. In each animal the trachea was occluded to about one-quarter of its normal diameter. Four of the animals showed almost no loss of weight; two a loss of 88 and 107 grm.; while one gained 54 grm. Sections were taken from the neck remnants and from the autotransplants (*Figs.* 101, 102). There was a definite reversion to the colloidal phase in both neck remnants and autotransplants in three of the animals. Of the other four, in one there was definite reversion in the autotransplants but only slight changes in the neck remnant; in another there was slight reversion to the colloidal phase in the autotransplant with definite reversion in the neck remnant; the changes in the other two were very slight or absent altogether.

DISCUSSION

These experiments have confirmed previous reports that after excision of one and three-quarter lobes of the thyroid, the remnant showed definite hyperplasia, and, further, that identical changes occurred in autotransplants when one of the excised lobes was transplanted.

It has also been confirmed that when the trachea is occluded to about one-quarter of its diameter an opposite change resulted, the colloid, or resting phase, being produced.

When both these procedures were carried out simultaneously the colloid phase predominated in some experiments, while hyperplasia occurred in others, the final histological picture apparently depending on which factor predominated.

It was thus possible by these simple surgical means to produce either hypertrophic or hypotrophic gland changes at will. The hyperplasia produced by subtotal resection is generally considered to be compensatory in character. The remnant left by excision hypertrophies to take on the work of the whole gland in order to supply the need for the body for thyroid secretion.

Breitner presumed that the colloid phase which followed partial tracheostenosis was due to a decreased oxygen intake, leaving less oxygen available for tissue oxidation, and thus a lowered metabolic rate. There was thus a lessened demand for thyroid secretion, resulting in the gland changing over to the hypoactive or colloid phase. Though metabolic rates have not been determined, this would appear a reasonable explanation, and, so far as is known, no experimental evidence has been brought to disprove Breitner's assumption. Consequently it is suggested that the thyroid gland changes histologically to hyperactive or hyperplastic type in response to increased body demand, and to the colloid or hypoactive phase when the demand is lessened.

A series of experiments were now undertaken to demonstrate whether or not the introduction of tracheostenosis would change a hypertrophic remnant to a colloidal type of gland. Hypertrophy was first produced by means of subtotal excision and confirmed histologically. Tracheostenosis was then instituted. When the animals were later sacrificed three of the six thyroid remnants showed definite reversion to the colloidal phase. The animals were healthy at death, none showing any great loss of weight; in fact, one showed a gain of 43 grm.

Similar changes from hyperplasia to the resting phase were next produced in autotransplants. This ruled out the possibility of the changes being due to

mechanical factors at the site of operation or to the influence of a nervous mechanism. The changes were evidently due to a blood-borne factor. In this set of experiments, in three animals there was definite reversion to the colloid phase in both remnant and autotransplants; in another the transition was marked in the remnant, but only slight changes occurred in the transplant; the opposite result was noted in the fifth animal, where the change was marked in the transplant but only showed up very slightly in the remnant; in the other two animals in this series only very slight, or negligible, changes occurred in both remnants and transplants.

Several variable factors have thus been shown to play a definite part in thyroid function. The importance of iodine, the most active constituent of thyroxine, has been shown repeatedly (Kendall, Lenhart, Loeb, Marine, et al.). Clinically the cellular, hyperplastic gland seen in Graves' disease changes to a colloid type when iodine is administered. Also, with regulation of iodine intake in hilly districts, colloid goitres have been greatly diminished in frequency.

A review of Collip's work, together with that of several other investigators who have produced thyroid changes by means of extracts of the anterior pituitary, demonstrates that antagonistic hormones are present in the blood which definitely regulate the activity of the thyroid gland, the thyreotropic hormone increasing it, whilst the antithyreotropic hormone decreases it. These changes are accompanied for the most part by changes in the thyroid to a hyperplastic or colloid type respectively.

We have endeavoured to show that these identical changes can be produced by increasing or decreasing the body demands on the thyroid. With a relatively increased demand, as produced by subtotal thyroidectomy, hyperplasia occurs; with a decreased demand, as produced by partial tracheostenosis, hypoplasia, or a colloid gland, is produced. It is therefore evident that in the normal control of thyroid function several factors play a part. Resulting from a change in body requirements at one end, definite changes occur in the gland at the other. That this occurs under normal physiological control is well recognized. Loeb observed differences in the degree of change during winter and during summer. During the growth period, menstruation, and pregnancy, the thyroid becomes more active owing to increased body requirements. These changes would appear to be under definite control of the finely balanced antagonistic thyreotropic and antithyreotropic hormones as demonstrated by Collip. The thyreotropic hormone originates in the anterior lobe of the pituitary; where the antithyreotropic hormone, which Collip has isolated from the blood serum, originates is not yet known. The stimulus leading to the production of these hormones, when body requirement is changed, may be transmitted through the autonomic nervous system.

As a result of an upset in the relationship between the thyreotropic and antithyreotropic hormones the thyroid is immediately affected, either becoming more active or less so. Since organic iodine, the most important constituent of thyroxine (Kendall), is lessened in the active gland and increased in the blood, as shown by Loeb, it is evident that the organic blood iodine must be affected during these changes. Whether the antagonistic thyreotropic and antithyreotropic hormones control the thyroid gland through the mobilization or immobilization of iodine is not known. Since the function of the thyroid is to produce thyroxine, it is more likely that the thyroid cells themselves have the specific property of controlling

the organic blood iodine and they in turn are under the governing influence of the thyreotropic and antithyreotropic hormones. Be that as it may, the following sequence of events appears likely to us. Since the demand for thyroxine becomes acute after subtotal thyroidectomy, there is an increase of thyreotropic hormone with resultant hypertropic changes in the gland and increased circulating thyroxine. Further, it is known that after six to eight weeks the compensatory hypertrophic gland reverts to the normal; now the antithyreotropic substance is increased with a diminution of thyroxine secretion as the body requirements are being met. During tracheostenosis there is a lessened demand for thyroxine which is reflected in an increase of antithyreotropic substance with lessened circulating thyroxine and consequent iodine storage. Similarly when tracheostenosis causes the compensatory hypertrophic gland to revert to the colloid phase there is an upset in thyreotropic and antithyreotropic hormones as a consequence of altered metabolic requirements. That there may be a hormone regulation in all these processes becomes apparent since we have demonstrated identical changes in autotransplants The chain of interrelationship between body requirements, antagonistic thyreotropic and antithyreotropic hormones, and iodine in physiologic thyroid control would appear to be established; for all three factors, under certain conditions, can produce identical changes in the histological picture of the thyroid.

SUMMARY

1. Extirpation of one and one-half to one and three-quarter lobes of the thyroid gland resulted in varying degrees of hypertrophy of the remnant, from a trace to marked hypertrophy.

2. Similar degrees of hypertrophy in autotransplants were noted.

3. Partial tracheostenosis of the trachea induced in guinea-pigs a colloid phase of the thyroid.

4. Removal of one and three-quarter lobes of the thyroid gland and simultaneous partial tracheal occlusion induced a colloid phase of the thyroid.

5. Reversion from the hypertrophic phase to the colloid phase of the thyroid gland occurred in neck remnants alone and simultaneously in both neck remnants and autotransplants.

6. These changes in thyroid histology are due to a blood-borne factor.

7. The close interrelationship between body requirements for thyroxin, thyreotropic and antithyreotropic hormones, and iodine has been established.

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CHOLECYSTOGRAPHY: ITS PRESENT CLINICAL VALUE

BY ROBERT McWHIRTER

CHIEF ASSISTANT, X-RAY DEPARTMENT, ST. BARTHOLOMEW'S HOSPITAL

THE object of this investigation was to attempt to find out the most reliable technique for cholecystography and to check the significance of various conclusions which have been based on the X-ray examination of the gall-bladder following the administration of sodium tetraiodophenolphthalein. The volume of material was relatively enormous, and accordingly it was hoped that the relative proportions of various pathological conditions would be more accurate than would have been the case if the investigation had been undertaken on a smaller number of cases. At the Mayo Clinic some five thousand gall-bladders are examined each year by the Graham dye test, and a large proportion are checked by operation, which can be the only profitable method of ascertaining the accuracy of the reports issued. It is interesting to observe, too, that all X-ray reports are based entirely on the films, the radiologist having no knowledge of the clinical condition of the patient except in those cases which have had previous operation on the gall-bladder. Following surgical intervention the operative findings and histological investigations are conveyed to the X-ray Department, and indeed it is not infrequent for a member of the X-ray staff to be actually present at the operation. By such careful co-operation between the surgeon and the radiologist an extraordinarily high degree of accuracy has been obtained.

The following points are considered in this paper: *(I) The roentgenological reporting of cholecystograms; (II) The technique of administration of the dye; (III) The analysis of the cholecystographic data for 1932 at the Mayo Clinic; (IV) The basis on which the diagnosis of tumours of the gall-bladder can be made; (V) Duodenal and gastric ulcer as a cause of non-filling of the gall-bladder; (VI) Disease of the liver as a cause of non-filling; (VII) The significance of delayed emptying; (VIII) The significance of calcium deposit in the gall-bladder; (IX) The frequency of carcinoma in cases with gall-stones.*

I. THE ROENTGENOLOGICAL REPORTING OF CHOLECYSTOGRAMS

In order to obtain a good cholecystogram, Barclay[1] has pointed out the conditions which must be present: (1) The salt must circulate in the blood in sufficient quantity; (2) The liver must be functioning actively and excreting the salt; (3) The mucous membrane of the gall-bladder must be sufficiently healthy to concentrate its contents.

In 1927 Caylor and Bollman[2] examined the relationship between the bilirubin content of gall-bladder bile and certain pathological conditions of the gall-bladder. The bilirubin content, determined by the van den Bergh method, of 105 gall-bladders removed at operation was compared with the pathological findings. From

this study they concluded that, in the majority of cases, the more disease there is present in the gall-bladder the lower is its bilirubin content. The important exception to this general rule is the gall-bladder with papillomata and associated hypertrophic rugæ; the significance of this finding will be discussed later.

From the above statement it might be considered that the density of the chole-cystogram, which like the bilirubin content depends on the degree of concentration of the bile, would be an indication of the extent of pathological change. In fact this method of estimating the amount of pathological change in the gall-bladder has been, and is still being, used in many X-ray departments, but so many disturbing factors have to be considered that from a practical point of view it cannot be used. For instance, the weight of the patient, the amount of absorption from the bowel (in the oral method), the presence or absence of sickness and diarrhœa, the size of the gall-bladder shadow (the larger the gall-bladder is, the less dense the shadow ought to be), the possibility of the fact that the gall-bladder has already commenced to empty or has not yet reached its maximum degree of concentration, would all require to be taken into consideration.

At the Mayo Clinic the following roentgenological reports are issued: (1) Normally functioning gall-bladder; (2) Normally functioning gall-bladder with stones; (3) Normally functioning gall-bladder with tumour; (4) Poorly functioning gall-bladder; (5) Poorly functioning gall-bladder with stones; (6) Non-functioning gall-bladder; (7) Non-functioning gall-bladder with stones.

The diagnosis of poorly functioning gall-bladder is made when the shadow of the gall-bladder as given by the dye is only just visible and where its density is less than that cast by the liver or kidney. This makes allowance for the variation in thickness of the patient, which has a very definite bearing on the density of the gall-bladder in the X-ray film.

The diagnosis of non-functioning gall-bladder indicates that the gall-bladder shadow is not visible at all or that the shadow is a primary one and has not increased in density by the administration of the dye.

Unless some such method is adopted the dividing line between normally functioning and poorly functioning gall-bladders becomes a very variable one, and at present it is almost impossible to compare the results obtained at different clinics.

The diagnosis of adhesions of the gall-bladder is frequently made, but Kirklin[3] has concluded from long experience that apparent deformity of contour is rarely a safe basis of diagnosis of disease. *Figs.* 103–106 support this view, and indicate that a gall-bladder may be markedly deformed merely by extrinsic pressure from the bowel, or depend on anatomical deformity.

When a cholecystogram is constantly of hour-glass shape it indicates anatomical deformity, as no disease in the wall can be found to account for this when the gall-bladder is examined histologically. *Figs.* 107 and 108 show gall-bladders which maintained their hour-glass shape throughout the period of investigation and were considered examples of anatomical deformity. Apparent hour-glass deformity may, of course, be due to extrinsic pressure from without, the most important cause being gas in the bowel.

In cases of previous cholecystostomy the fundus of the gall-bladder is often blurred and indistinct, and an example of this is given in *Fig.* 109. It is worthy of note at this point that the gall-bladder in men of sthenic build usually lies horizontally with the fundus to the right (*Fig.* 110).

FIG. 103.—Apparent cutting off of lower end of gall-bladder. The next film showed a normal gall-bladder.

FIG. 104.—Deformity of medial side of gall-bladder shadow produced probably by the duodenal cap.

FIG. 105.—Marked deformity. Gall-bladder normal at operation.

FIG. 106.—Apparent example of bifid fundus—the next photograph showed that the outline was normal.

FIG. 107.—Hour-glass deformity due to anatomical causes.

FIG. 108.—Double hour-glass deformity also due to anatomical causes.

FIG. 109.—Note blurring of fundus : this patient had a cholecystostomy in 1909

Perhaps it would be interesting to state here that in addition to the diagnosis of adhesions of the gall-bladder in cholecystograms not being made, the diagnosis of adhesions to the duodenal cap is also not made at the Mayo Clinic. That such a condition exists is not disputed, and Rowden[1] has described the 'dunce's cap deformity' of the duodenum, which suggests adhesions to the gall-bladder. Thousands of duodenal caps are examined in the Mayo Clinic each year and an accuracy in the diagnosis of duodenal ulcer of over 98 per cent has been obtained —that is to say, 98 per cent of all persistently deformed duodenal caps have been proved by operation to be due to duodenal ulcer. Of the small proportion remaining (less than 2 per cent) the commonest cause was certainly gall-bladder adhesions, but since no important difference could be detected between those two types of
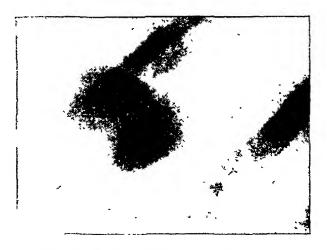
FIG. 110.—Example of gall-bladder in a patient of sthenic build. Note the viscus lies almost horizontally.

deformity the diagnosis of adhesions was abandoned. Attempts to arrive at this conclusion only increased the percentage of errors instead of diminishing them. Accordingly all persistently deformed duodenal caps are considered to be due to ulcer. When considered from the cholecystographic aspect very markedly deformed shadows have been found repeatedly at operation to be associated with a perfectly normal viscus. On the other hand, when adhesions are present the gall-bladder outline may be quite normal. Kirklin,[4] on examining 204 gall-bladders which appeared normal from an X-ray point of view, found that no fewer than 40 cases at the time of operation were associated with adhesions. From the above considerations it follows that even combined gall-bladder and barium meal investigation has been considered to be of little value in arriving at a diagnosis of adhesions between the gall-bladder and the duodenal cap.

II. TECHNIQUE OF ADMINISTRATION OF THE DYE

There are two main methods of giving the dye : (1) The intravenous ; (2) The oral. Considerable controversy has arisen concerning which of the two methods is the better, and the dispute is not yet settled. At the Mayo Clinic the oral method

is the only one employed, and I hope to show that the results so obtained are of such a high order of accuracy that they at least equal those obtained by the intra-venous method. But the oral technique is often faulty, and in order to obtain good results certain important points must be carefully observed. Kirklin[3] insists on the following points :—

1. The dye must be given in sufficient quantity. He recommends 4 grm. as the standard dose for all adult patients regardless of their weight. A reduction is only made in the case of children under fifteen or sixteen years of age.

2. The dye must be given in a readily absorbable form. The use of capsules, etc., has not been found to be necessary, and the capsules may not be absorbed and the dye remain enclosed.

3. The dye must be given in such a manner that it will not produce undue nausea and vomiting. Many persons can take the dye in simple aqueous solution, but some become nauseated or object to the taste. If there is doubt, 2 to 3 gr. of luminal one hour before the meal will prevent sickness and in addition will tend to check diarrhœa. Between four and six thousand cholecystograms are made in the Mayo Clinic each year and experience has shown that those two objections are in the main surmounted by giving the dye in a glassful of fruit-juice or carbonated water. Grape-juice is preferred. The frequent practice of giving the dye on an empty stomach has been abandoned, and it has been found best to give the dye immediately after a full meal, and this meal should contain a minimum of fat.

4. The dye must be given under conditions that will not hamper its evacuation from the stomach, its absorption from the bowel, or its accumulation and concen-tration in a normal gall-bladder. If a fatty meal is given with the idea of emptying the gall-bladder of the bile it already contains, the error in diagnosis is increased because fat greatly delays evacuation from the stomach. Levyn[5] observed that when a fatty meal immediately preceded barium examination there was almost invariably a six hours' gastric residue. Consequently there will be delay in evacua-tion of the dye from the stomach, and the prolonged flow of fatty foods through the duodenum will interfere with concentration in the gall-bladder. Delarie,[6] too, has shown that in animals fat renders a greater amount of the dye in the small bowel insoluble.

Absorption from the bowel is interfered with by giving purgatives, and enemata on the morning of the examination have been found satisfactory in emptying the colon. Objections have been raised to the administration of an enema because, it is alleged, one cannot tell how much dye has remained unabsorbed in the colon. Obviously this is of no importance, for if the gall-bladder is healthy it will have absorbed as much dye as it can, and if on the other hand it is pathological it will not absorb any, and in either case only the unabsorbed dye will be seen in the colon. However, an enema is not always necessary, and its administration can be conveniently postponed till after the first film.

This method, employing the above essential principles, has been in use at the Mayo Clinic for more than three years. The details of the examination are as follows :—

The patient receives 4 grm. of sodium tetraiodophenolphthalein (the pure drug is used) dissolved in 30 c.c. of distilled water and is given the following printed instructions :—

a. At 6 or 7 p.m. eat supper of the usual amount, but without cream, eggs, butter, or other fats.

b. Immediately after supper empty the entire contents of this bottle (the dye) into a glassful of grape-juice, stir well, and drink all.
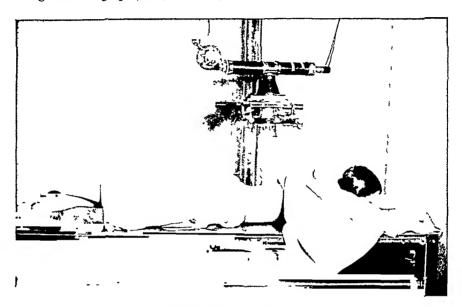
FIG 111—Position normally assumed by patient on table   Note uncomfortable attitude and incomplete relaxation of muscles
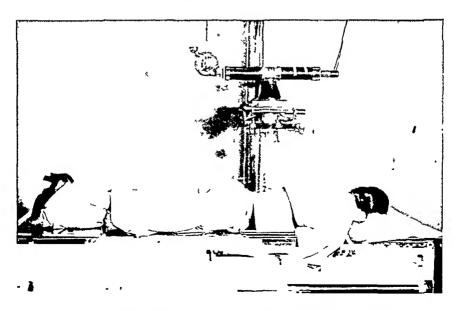
FIG. 112—Position in which patient should be placed. Note comfortable position of head and arms, and pillow under ankles   The canvas band aids in immobilization.

c. Do not take a laxative or any other medicine.

d. At 7 o'clock next morning take a rectal injection of warm salt solution until the water returns clear.

e. Do not eat breakfast; *you may drink water, black coffee, or clear tea.*

Films (anterior views only) are taken at the fourteenth and sixteenth hours after the dye and again at the twentieth hour, the patient having partaken of lunch with a glassful of cream and milk in equal parts three-quarters of an hour prior to this last examination.

At the time of examination it is essential in order to avoid movement that the patient be placed comfortably on the X-ray table, which is equipped with a flat Potter-Bucky grid. He lies with his cheek to the pillow, his arms forward, and his ankles supported by a cushion. To secure thorough immobilization a broad canvas band is drawn tightly over the back (*Figs.* 111, 112). The picture is taken in expiration, and the exposure should not exceed one-half to one second, so as to avoid movement of either the patient or the gall-bladder by peristaltic movements of the bowel. *Figs.* 113–115 show how the shadows of gall-stones can be completely obliterated by slight movement. Recently at St. Bartholomew's Hospital films in the erect posture have been taken routinely in addition to prone films. So far no advantage has been obtained. It has been stated that it is possible to observe small stones which fall to the fundus and which would not have been visible otherwise. But it would seem unnecessary to do this, for with careful technique and the aid of the fatty meal very tiny stones can be detected (*see Fig.* 138). Moreover, it is more difficult for the patient to keep steady in this position. It may, however, be of value in differentiating between a stone and a tumour.

The first roentgenogram is inspected for errors of technique, and if the gall-bladder is obscured by gas, the technician massages the abdomen to displace the gas or requires the patient to repeat the enema. If the shadow is obscured by the ribs, subsequent films are taken in inspiration and the tube may be decentred to throw the gall-bladder clear of the spine. *Figs.* 116 and 117 show how the gall-bladder may be separated from the colon shadow by suitable compression.

As already mentioned, it is very difficult to compare the results obtained at different clinics because of the variation in the definition of the terms ' normally' and ' poorly-functioning' gall-bladder. The intravenous method, employed by Graham,[7] has given excellent results, but when compared with the results obtained by Kirklin[3] they cannot be said to be better. In order, however, to be able to make a fair comparison between the two methods it is essential to compare the accuracy obtained in the same clinic where the two methods have been used.

Some time ago Kirklin[3] checked a series of cases of non-filling of the gall-bladder when the oral method had been used, by intravenous injection of the dye, and found the increase in filling was about 1 per cent. In addition he showed that if the cases of non-filling had the oral method repeated, the increase of filling of the gall-bladder was 1 per cent. Consequently it would appear that the oral method as employed by Kirklin will give a cholecystogram in as many cases as the intravenous, if those cases which do not fill on the first examination have the oral method repeated. It is the practice at the Mayo Clinic to repeat the oral administration of the dye in twenty-four hours if no shadow is obtained at the first examination.

Hawley[8] also compared the results obtained in 265 cases examined by the oral technique with 235 cases in which the intravenous method was used. The cases
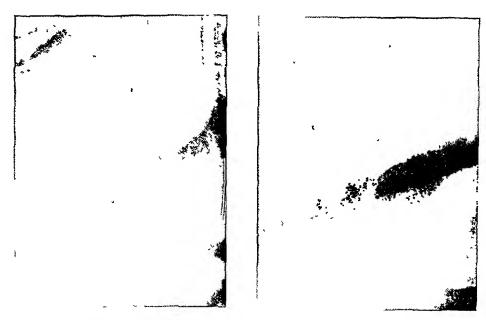
FIG 113.—Note shadow of large gall-stone.

FIG 114 —Same patient as shown in *Fig* 113 · no gall-stone is visible now ; patient has moved slightly.
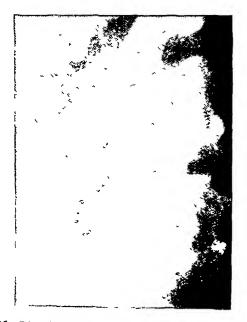
FIG. 115 —Film where the stones could easily be missed by movement.

were selected at random. It is important to realize, however, that his method of oral administration varied somewhat from that of Kirklin. Nevertheless, and in spite of the fact that he began the investigation with the idea that the intravenous method was superior, he concluded that the oral method was as accurate as the intravenous, and finally adopted the former as his method of investigation for future

FIG. 116.—Gall-bladder hidden by colon. No stones visible.
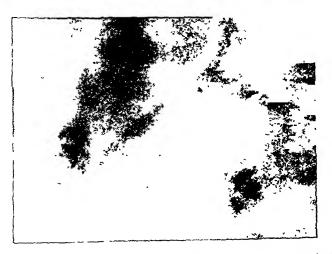
FIG. 117.—Same case as *Fig.* 116 : stones now visible. This film was taken after a compression band had been drawn tightly over the lower ribs. An alternative method would have been to administer an enema.

cases. (The proved errors were 9 per cent in the intravenous and 10 per cent in the oral method.)

Certainly the intravenous route of administration is now almost entirely free from serious complications, but if any of the dye is accidentally injected into the tissues around the vein, necrosis and sloughing of the subcutaneous tissues may result, with great dealy in healing. Intravenous injection can often be tedious and troublesome, and in difficult cases may necessitate cutting down on the vein.

The whole process is naturally a greater ordeal to the patient than the oral method, and if results can be obtained by the latter method which are as good, the oral method is certainly the one of choice.

Contra-indications to Employment of Graham Test.—Cholecystography should not be used in patients suffering from obstructive jaundice, because fatal pancreatitis has sometimes followed such cases (Choyce and Beattie[9]).   In acute cases Hawley[8] concluded that the information gained is not worth the suffering because the dye upsets these patients very much.   On the other hand, in cases of chronic cholecystitis Nickel and Judd[10] have shown that sodium tetraiodophenolphthalein on entering the gall-bladder has a bacteriostatic influence on the organisms it contains, so that the administration of the dye may be actually beneficial in those cases.

III. ANALYSIS OF CHOLECYSTOGRAPHIC DATA FOR 1932

During 1932 at the Mayo Clinic 4676 patients were examined by the use of cholecystography and 732 were operated on.   The cholecystographic diagnosis, whether positive or negative, was confirmed in 696 out of the 732 cases (95 per cent).

CHOLECYSTGRAPHIC DATA FOR 1932

DIAGNOSIS	CASES	FINDINGS AT OPERATION								DIAGNOSIS CONFIRMED AT OPERATION
		Gall-stones	Tumours	Cholecystitis Grade				Miscellaneous	Normal	
				Not graded	2	3	4			
Normally functioning gall-bladder	287	4	2	19	4		1		257	Per cent 89·5
Poorly functioning gall-bladder ..	39	28 (71·8%)		5		1	2	1	2	94·8
Non-functioning gall-bladder ..	106	90 (84·9%)	3	4	3		2	1	3	97·1
Normally functioning gall-bladder with stones 124										
Poorly functioning gall-bladder with stones 78	294	293	1							99·6
Non-functioning gall-bladder with stones 92										
Tumour	6			6						100·0
Total ..	732	415	12	28	7	1	5	2	262	

445 cases with positive cholecystographic data; 6 errors (98·6 per cent correct). Of 732 diagnoses, 696 (95·0 per cent) were confirmed.

415 cases with gall-stones at operation; 411 (99·0 per cent) with positive cholecystographic data. Of the 415 cases, gall-stones were visualized and reported in 294 (70·8 per cent).

470 cases with disease of the gall-bladder at operation; positive cholecystographic data in 440 (93·6 per cent).

262 cases without disease of the gall-bladder at operation; negative cholecystographic data in 257 (98·0 per cent).

Among 287 patients with normal cholecystograms who were operated on, chiefly for diseases other than that of the gall-bladder, surgical exploration confirmed the cholecystographic diagnosis in 257 (89·5 per cent). It is well known that the highest percentage of errors is caused by diseased gall-bladders which maintain their function sufficiently to produce a normal shadow. If the intravenous method gave a higher percentage of filling of the gall-bladder, the percentage of errors would be increased.

Of 445 patients with positive cholecystographic data, 439 (98·6 per cent) had gall-bladder disease. In 415, gall-stones were found at operation, and of these cases the evidence of the cholecystographic data showed a pathological condition of the gall-bladder in 411 (99 per cent), gall-stones as such being diagnosed in 294 (70·8 per cent). In 6 cases in which a diagnosis of tumour of the gall-bladder had been made the diagnosis was confirmed, but papillomas were also found in a few cases in which this specific diagnosis had not been made.

It will be seen from the table that gall-stones can be recognized in a very high percentage of cases (70·8 per cent). Moreover, their presence can be suspected in a still higher number of cases, for 71·8 per cent of the poorly-functioning and 84·9 per cent of the non-functioning gall-bladders were found to contain stones. This represents a very real contribution to diagnosis, because before the use of the dye test Pfahler[11] in 1914 gave 50 per cent as the average of cases of gall-stones in which the calculi could actually be seen on the plain film. This figure of 50 per cent is probably considerably higher than is usually stated in this country, for Choyce and Beattie[9] gave only 20 per cent, and Rowden[12] stated that not one in ten cases of stones was visible before the dye test was used. (*Figs.* 118–120.)
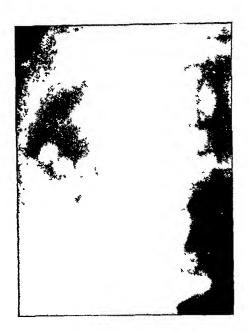
The Interpretation of the Term ' Poorly-functioning ' Gall-bladder without Stones in Terms of Pathology.—A series of 45 cases checked by operation is given and was made up as follows :—

Cholecystitis with gall-stones	35
Cholecystitis	6
Cholecystitis with papilloma	2
Carcinoma of pancreas	1
Gall-bladder normal	1

The Interpretation of the Term ' Non-functioning ' Gall-bladder without Stones in Terms of Pathology.—In this group a series of 112 cases checked by operation are considered :—

Cholecystitis with gall-stones	95
Cholecystitis	7
Carcinoma of the gall-bladder	1
Carcinoma of ampulla of Vater	1
Carcinoma of ducts with stones in gall-bladder	1
Fistula of the gall-bladder	1
Stones in the common bile-duct only	1
Cholangitis	1
Congenital absence of the gall-bladder	1
Carcinoma of pancreas	1
Gall-bladder normal	2

It will be readily observed from the above tables that by far the commonest cause of poorly-functioning and non-functioning gall-bladders is cholecystitis with gall-stones. It will also be noted that two cases of carcinoma of the pancreas are included in those tables. This is interesting, especially when the case of stone

FIGS 118, 119 —Radiotranslucent stones, or 'negative shadows', which would not be visible without dye.

FIG 120 —An enormous number of radiotrans-
lucent stones Generally in such a case no contrast
filling is obtained and the gall-bladder falls into the
non-functioning group
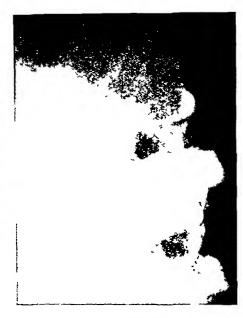
FIG 121 —Double gall-bladder
(*By courtesy of Dr E W. Twining*)

in the common bile-duct is also considered, for it would appear that obstruction to the outflow of bile interferes with the production of a shadow. Probably the increased pressure so damages the liver that it ceases to function, for it is a well-known surgical finding in cases of long-standing obstruction that the biliary system is filled with clear fluid and not with bile. This so-called ' white bile 'may indeed be the only part of the body which is not stained yellow. The explanation of the phenomenon lies in the fact that the bile is absorbed from the gall-baldder and ducts and the pressure is too high for the liver cells to function. But the glands lining the common bile-duct can secrete this clear fluid under a slightly higher pressure and so the duct system becomes filled with their secretion. In view of this occurrence, then, non-filling of the gall-bladder with dye is what one would expect.

Congenital absence of the gall-bladder of course is rare. One case exists in the London Hospital Museum. Another example of congenital abnormality is duplication (*Fig.* 121), which may be complete, as in the case reported by Sherren,[13] or the gall-bladder may have merely a bifid fundus. Congenital absence of the bile-ducts is not a radiological problem for the child dies soon after birth. Fistula of the gall-bladder will obviously prevent formation of a shadow.

Examples of Possible Errors in Diagnosis.—

1. Calcification of the rib cartilage. Doubt is easily removed if pictures are taken in inspiration and expiration, and it will then be seen that the calcified area does not move with the gall-bladder shadow.

2. Opaque material in bowel. This type of shadow will vary in position in the different films and may be absent in one or two of the films (*Fig.* 122). Opaque material in diverticula of the transverse colon has been considered as a possible source of error in diagnosis by Potter.[14]

FIG 122 —*Opaque material in bowel superimposed on faint gall-bladder shadow A subsequent photograph showed material to the left of the middle line and apparently in the transverse colon*

3. Renal stones are easily recognized as being distinct from the gall-bladder shadow and as moving with the kidney shadow.

4. The cystic gland lying in the angle between the cystic duct and the common hepatic duct may calcify and simulate a stone, but the shadow is again apart from the gall-bladder shadow. To differentiate it from a stone in the common bile-duct it is well to remember that obstruction of the duct will almost certainly lead to the gall-bladder not filling, and should it fill at all, the shadow will be faint and of increased size. Moreover, the patient will have jaundice. In certain cases, either by the aid of the fatty meal or by the use of compression, it may be possible to demonstrate the common bile-duct. (*See Figs.* 129–131.)

5. Pancreatic calculi are very rare, only some forty cases having been described in the literature (Lindsay[15]).

6. Superficial tumours of the skin are best ruled out by inspection of the skin of the patient prior to X-ray examination.

7. Calcification of the right adrenal gland should not be confused with calcification of the gall-bladder wall or a calcified stone. Examples of this are given in an article by Camp, Ball, and Greene.[16]

8. Mention has already been made of the danger in drawing conclusions from distortion and irregularity of the contour.
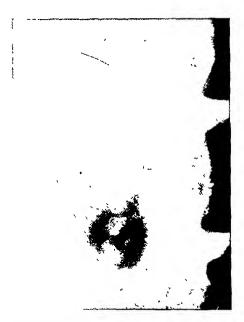
FIG. 123.—Gas in bowel superimposed on gall-bladder shadow and simulating radiotranslucent stones.

FIG. 124.—Radiotranslucent stones very similar to gas-bubbles in previous photograph.

9. Gas-bubbles in the bowel superimposed on the gall-bladder may closely simulate stone, but the diagnosis can generally be cleared up by viewing all the films and noting the variation in the shape, size, and position of the gas-bubbles. It would almost appear that the radiologist is more apt to consider a radiotranslucent stone to be a gas-bubble than vice versa (*Figs.* 123, 124).

10. The differential points between tumour of the gall-bladder and stone are given later.

IV. THE BASIS ON WHICH THE DIAGNOSIS OF TUMOUR OF THE GALL-BLADDER CAN BE MADE

Tumours of the gall-bladder were first recognized by Kirklin,[17] and their recognition was due to the careful system of checking all cases that have passed through the X-ray department—a system which unfortunately in this country is often only half-hearted.

In 1930 a small rounded radiotranslucent shadow near the fundus was interpreted as being a gall-stone, but at operation an adenoma was found. This stimulated further investigation, and now a diagnosis of tumour is frequently made at the Mayo Clinic and with an amazing degree of accuracy. Tumours as small as 1 mm. in diameter have been reported, and that this has become possible, together with the differentiation of so tiny a tumour from a stone, is a very high tribute to the excellence of the technique and the care taken in the reporting of films. But a stage further even than this high standard has now been reached, and adenoma can often be distinguished from papilloma.

Both benign and malignant tumours occur in the gall-bladder.

Benign Tumours.—The following benign tumours are described in the gall-bladder: (1) Papilloma; (2) Adenoma; (3) Fibroma; (4) Lipoma; (5) Myoma. Occasionally a piece of aberrant liver is found adhering to the wall of the gall-bladder and this may simulate a tumour. Papilloma and adenoma are the only tumours which have been detected so far by X-ray examination.

Papillomata.—Papilloma is by far the commonest simple tumour, and in 17,000 gall-bladders surgically removed at the Mayo Clinic papillomata were found in 8·5 per cent of those cases. Kaufmann[18] believes that the older a person gets, the more papillomatous the gall-bladder epithelium tends to become. These papillomata are of two types: (1) The true neoplasm; (2) The polypoid cholesterol-laden villus. The latter type is the commoner and has no tendency to become malignant. The former type when multiple, however, must be regarded as potentially malignant.

The enlarged polypoid cholesterol-laden villus is really an example of localized cholesterosis (strawberry gall-bladder). They are generally accompanied by marked hypertrophy of the epithelial lining of the gall-bladder, and Erwin and MacCarty[19] pointed out that this epithelial hyperplasia is the most striking characteristic of chronic cholecyctitis with papillomata. Caylor and Bollman[2] found that such gall-bladders gave the highest concentration of bilirubin. Stones may be present in addition and are frequently of the cholesterol variety. Boyd,[20] in fact, has suggested that a broken-off polyp may form the nucleus of a stone in strawberry gall-bladders. From the records of the Mayo Clinic the diagnosis of strawberry gall-bladder by itself would appear to be impossible.

Rossi[21] claims that strawberry gall-bladder can be identified by the following signs. The filling of the viscus is slow and emptying is always delayed. There is pain on palpation and certain ‘indirect signs’. But his observations are not convincing.

The origin of the cholesterol in these villi is stated by Andrews, Schoenheimer, and Hrdina[22] to be from the blood-stream and not from the biliary cholesterol as is frequently believed. The condition then becomes comparable to xanthoma of the skin and atheroma of blood-vessels.

Papillomata generally have a diameter of less than 0·5 cm. and rarely exceed 1 cm. They are more often multiple than single.

Kirklin[17] has given the radiographic characteristics of papillomata as follows (*Figs.* 125–128):—

    1. They have the same relative position even at re-examination.

    2. Defects are generally clear, rounded, and small, and usually less than 0·5 cm. in diameter.

FIG. 125.—Shadow defect on medial wall of gall-bladder due to papilloma.
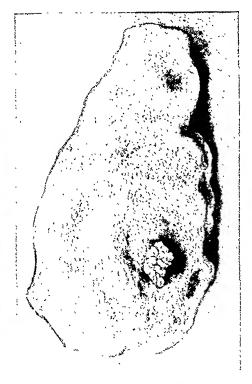
FIG. 126.—Photograph of this gall-bladder laid open to show papilloma.

FIG. 127.—Multiple radiotranslucent areas due to papillomata fourteen hours after dye.

FIG. 128.—Same gall-bladder as *Fig.* 127 after removal, showing one large and several small papillomata.

3. They do not tend to occur immediately at the pole of the fundus and a marginal position is especially suggestive.

4. They are generally multiple.

5. When multiple the defects are well separated and never grouped closely like gall-stones.

6. They are generally most plainly visible at the twentieth hour and may only be visible at this time.

7. The cholecystogram is generally good or above average density—this is in accordance with the findings of Caylor and Bollman[2] on bilirubin content of such gall-bladders.

Adenomata (Figs. 129–135).—The following are the chief points in the diagnosis of adenomata :—

1. They generally occur directly at the pole of the fundus.

2. They are generally larger than papillomata. Average size 8 mm.

3. They are generally single. Of 61 cases of adenoma recorded at the Mayo Clinic between 1927 and 1931 all were single except two cases.

4. They are always sessile.

5. They are frequently associated with gall-stones ; 34 cases out of the series of 61 had gall-stones, and cholecystitis was noted in 44 cases.

6. They are seldom visible till the twentieth-hour film, although their presence may be indicated in the earlier films by a fine slit-like defect at the fundus.

In a series of 47 cases examined cholecystographically normal density was noted in 23 cases and a faint shadow was observed in a further 9 cases.

On removal of the gall-bladder they can be seen as a small button-like prominence in the region of the fundus.

Differential Diagnosis of Simple Tumours from Gall-stones.—Gall-stones are : (1) Variable in situation ; (2) Grouped closely, especially as the gall-bladder contracts ; (3) Faceted and angular ; (4) They may have a calcium coating ; (5) Even without a calcium coating they are less clearly transparent than tumours.

Malignant Tumours.—These are generally carcinomata. Sarcoma is rare. Kaufmann[18] could find only 13 cases reported in the literature.

In a series of 22,365 operations at the Mayo Clinic on the gall-bladder and biliary tract Judd and Gray[23] found primary carcinoma of the gall-bladder in 212 cases ; 74 per cent of these cases occurred in the female, so that carcinoma and gall-stones display the same sex ratio. Zenker[24] reported 72·9 per cent in females, Naunyn[25] 83 per cent, and Musser[26] 75 per cent.

The youngest patient was 23 years and the oldest 78 years, and 73·4 per cent of the cases occurred between the ages of 50 and 70 years. Stones were associated in 64·6 per cent of cases.

The carcinoma may originate at the fundus or near the cystic duct, and the gall-bladder may rapidly be filled by tumour tissue, or if the carcinoma is of the scirrhous type the walls are contracted and the lumen is obliterated. Again, when it originates near the cystic duct this becomes blocked. These factors probably in the main account for the fact that where carcinoma of the gall-bladder has been found at operation or post-mortem the X-ray report has been ' non-functioning gall-bladder '.

At the Mayo Clinic, of 16 cases examined cholecystographically 14 gave no shadow of the gall-bladder although stones were visible in 7, one case was normal

FIG 129 —Note excellent shadow of gall bladder
Adenoma not visible

FIG 130 —Same case as *Fig* 129 twenty minutes
later Gall-bladder partially emptied Adenoma
becoming visible

FIG 131 —Same case as *Fig* 129 one hour after first
film Adenoma plainly visible

FIG 132 —Same as *Fig* 129, one and a half hours
after first film
This series of photographs shows the great value
of the fat meal in rendering visible the tumour
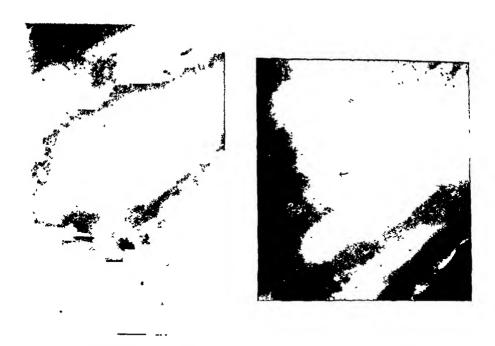
FIG. 133.—Gall-bladder lying transversely. No adenoma visible.

FIG. 134.—Same case as *Fig.* 133 after administration of fat meal. Adenoma only now visible.
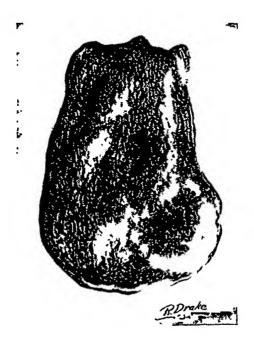
FIG. 135.—Same gall-bladder as that shown in *Fig.* 134 laid open to show adenoma at fundus.

with stones, and one gave a normal shadow in which no defect could be distinguished.

Rowden[1] met with the condition only twice—in one case he detected two large stones, and in the other the gall-bladder failed to fill.

Taterka[27] reported a case with a defect in the wall which at operation proved to be a carcinoma, but apart from this one case all other attempts by cholecystography to reveal malignant tumours have failed.

Kirklin[17] has suggested that a defect which is constant and has a diameter more than 2 cm. with an irregular internal border should make the examiner suspect carcinoma. At the best it can only be hoped to detect early cases.

Carcinoma involving the extrahepatic ducts is less frequent, there being only 100 cases in the series of Judd and Gray[23] (22,365 operations), and appears to be more frequent in the male (58 per cent, Judd and Gray,[23] and 61 per cent, Rolleston[28]). In the two cases in the 1932 group examined at the Mayo Clinic cholecystographically both were associated with non-functioning gall-bladder. One of the cases was a carcinoma of the ampulla of Vater, and it is just possible that had irregularity of the second part of the duodenum been found on barium meal examination in association with a non-functioning gall-bladder, a diagnosis of carcinoma of the ampulla of Vater could have been suggested. Carcinoma of the ampulla of Vater has been raised to the status of a definite clinical entity, and Gustav Pallin[29] has collected 16 cases.

V. DUODENAL AND GASTRIC ULCERS AS A CAUSE OF NON-FILLING OF THE GALL-BLADDER

Brailsford[30] and others have stated that in a certain number of cases of gastric and duodenal ulcer the gall-bladder fails to fill satisfactorily, and suggest that an opaque meal should be given in all non-functioning cases.

In a series of 184 operations on non-functioning gall-bladders duodenal ulcer was found in only 2 cases. One of these cases was associated with gall-stones and cholecystitis, and in the other I could find no report on the state of the gall-bladder, which was therefore presumably normal.

In a series of 127 cases of poorly-functioning gall-bladders duodenal ulcer was found in only 4 cases. Of these, 3 had associated stones and 1 had no gall-bladder lesion.

On the other hand, in a series of 350 investigated cases of normally functioning gall-bladders duodenal ulcer was found at operation in 60, or 17 per cent of the total.

In 1927 Kirklin[4] analysed 204 normally functioning gall-bladders and found :—

Duodenal ulcer	..	..	..	.. 78
Gastric ulcer ..	..	..	..	.. 5
Gastric and duodenal ulcer	..	..	..	.. 5
Gastric carcinoma	..	..	..	.. 2

Out of 1398 cases of good visualization, Ferguson and Palmer[52] found 209 cases of duodenal ulcer and 14 cases of gastric ulcer, giving a total of 16 per cent of cases with good shadow and ulceration of the duodenum or stomach.

The above data would appear to show that lesions of the stomach and duodenum play no part in interfering with the filling of the gall-bladder with dye. It is true that several series of cases have been reported from time to time in which

duodenal ulcer was found associated with gall-bladders that did not fill, but it must be remembered that most of the cases in which cholecystograms are made are patients who are suffering from indigestion, and the proportion of duodenal ulcers will be high.   Certainly the above figures show a far higher percentage of duodenal ulcers in the cases in which the gall-bladder filled normally.

In cases of gross pyloric obstruction there may be delayed absorption of the dye and poor filling.   In many of these cases, however, the dye can be seen in the stomach, casting a faint ill-defined shadow, and the radiologist's suspicions will be aroused.

VI. DISEASE OF THE LIVER AS A CAUSE OF NON-FILLING OF THE GALL-BLADDER

Barclay[1] has stated that one of the requisites for satisfactory filling of the gall-bladder by the Graham test is that the liver is functioning actively and excreting the salt.   It is important to note that it is not necessary for the liver to be healthy and free from disease in order to do this, as is sometimes stated.   So long as sufficient healthy liver tissue remains, a good cholecystogram should be obtained— probably only a small amount is necessary.

Of 219 cases of normally-functioning gall-bladder examined at the Mayo Clinic by operation, 3 cases were found in which the liver was seriously diseased. One showed a carcinoma of the liver, one was a case of cirrhosis, and the third was a case of splenic anæmia with associated hepatic cirrhosis.

Ferguson and Palmer,[52] in a series of 1398 cases of good visualization, found : 1 case of atrophic cirrhosis, 8 cases of catarrhal jaundice, and 3 cases of neoplasm of the liver.

In one case of may own the patient had slight jaundice at the time of examination and died some ten days later from subacute yellow atrophy, and yet the cholecystogram was of very good density.

VII. SIGNIFICANCE OF DELAYED EMPTYING OF THE GALL-BLADDER

Delayed emptying of a dye-filled gall-bladder is often considered as evidence of disease.   In the first place it would seem likely that a gall-bladder which fills will always be capable of emptying.

Apart from this, when a gall-bladder does empty, the dye will pass into the bowel and then be re-absorbed and carried to the liver again just as the bile-salts are in the so-called entero-hepatic circulation.   In fact a gall-bladder can be followed till it empties completely of dye, and provided the dye is not all got rid of by evacuation of the bowel it can be observed to appear again in the gall-bladder.

The logical conclusion to be drawn from a gall-bladder that remains filled for some time would appear to be that the patient has constipation and that the gall-bladder is healthy.   Yet many radiologists still give a fat meal in order to see how rapidly the gall-bladder empties, and fail to realize that the purpose of this meal is to cause the gall-bladder to contract and so render visible small stones and tumours.   As has been mentioned previously, adenomata rarely show till after the fat meal has been given (see Figs. 129–132).

Ivy and Oldberg[31] have succeeded in producing contraction of the gall-bladder by injection of an extract of intestinal mucosa which they call 'cholecystokinin', and suggest that the fatty meal may stimulate the production of such a substance.

VIII. THE SIGNIFICANCE OF CALCIUM DEPOSIT IN THE GALL-BLADDER

Calcium is found deposited in stones, sometimes as the nucleus but more often as a ring enclosing a radiotranslucent stone, in the wall of the gall-bladder, or as amorphous calcareous débris in the interior of the viscus.

Romang[32] has shown by analysis of radiopaque material from the gall-bladder that this is almost always calcium carbonate, since calcium phosphate is present only in small amounts. Calcium bilirubinate stones contain so very little calcium that their absorption of X rays is only a little greater than that of water, while calcium carbonate is fifteen times greater than water.

In the case of stones the deposition of calcium in rings with the growth of the stone in the intervals between the rings, due to cholesterol and pigment, suggests that some very definite change must have occurred in the chemical composition of the gall-bladder contents. The most likely cause of this change is blockage of the cystic duct, and the following evidence seems to support this view.

A. L. Wilkie[33] carried out a series of interesting experiments on rabbits in the Surgical Research Department of the University of Edinburgh. The cystic duct was carefully ligated and streptococci were injected into the wall of the gall-bladder. When the animal was killed some time later the wall was thickened and fibrous, and the contents consisted of mucopurulent material with granular débris and calculi which contained a considerable quantity of calcium. On the other hand, when the experiment was repeated but the cystic duct left patent, the stones that formed were made up mainly of cholesterol and no calcium was found. (It is only fair to state, however, that Wilkie's work has been adversely criticized by Williams and McLachlan[34] and has not been confirmed.)

Johnston, Ravdin, Austin, and Morrison[35] studied the absorption of calcium from the bile-free gall-bladder. Dogs were used and the cystic duct was ligated but the vessels and lymphatics were left intact. They reported from their observations that they would conclude that calcium is not secreted into the gall-bladder when the wall is normal, but that a small amount may be secreted when the viscus is damaged.

Phemister, Day, and Hastings,[36] from experiments on animals, concluded that the requirements necessary for the deposition of calcium in the gall-bladder were: (1) Obstruction of the cystic duct; and (2) Low-grade chronic inflammation. They further state that the chemical composition of the gall-bladder contents under these circumstances becomes altered and calcium accumulates to such an extent that supersaturation results and the calcium is deposited.

Blockage of the duct may occur by impaction of a stone either in the duct itself; or in Hartmann's pouch (a lateral pouching at the junction of the cystic duct and gall-bladder); or by inflammation, for the cystic duct is 1½ in. long and is only ¼ in. in diameter, and its lumen is further narrowed by Heister's valves; or lastly by tumour originating in the vicinity of the outlet.

Phemister, Rewbridge, and Rudisill[37] reported seven cases of calcium carbonate

deposit in the wall of the gall-bladder, the cystic duct of which was obstructed by stone or inflammation in every instance, and stated that there is generally no bile in such gall-bladders. The bile is probably all absorbed just as it is in those cases already mentioned in which the common bile-duct is obstructed and 'white bile' is formed.

Whipple,[38] of New York, reported a case of calcium carbonate paste in the gall-bladder, the cystic duct of which was obstructed by carcinoma.

Fowler[39] reported a case of calcified gall-bladder with complete obstruction of the cystic duct.

Grey Turner[9] states that calculi with a large proportion of calcium are most frequently formed in closed infected gall-bladders.

Volkmann[40] suggests that in cases of 'Kalkmilchgalle' (lime-water bile), the calcium may have been secreted by the gall-bladder when the cystic duct is obstructed.

FIG. 136.—Note the stone in the cystic duct and no dye in the gall-bladder.

Phemister, Rewbridge, and Rudisill[37] reported three interesting cases in which a stone blocked the cystic duct and calcium was deposited only on the gall-bladder side of the stone.

Phemister, Day, and Hastings[36] studied 11 cases of obstruction of the cystic duct and found that 6 had mild chronic cholecystitis with a separate deposit of calcium carbonate in the gall-bladder. The remaining 5 cases had no calcium carbonate precipitation but showed more marked inflammation with serous exudation and the ordinary picture of hydrops.

The above references show that cystic-duct obstruction and calcium deposition in the gall-bladder are frequently found associated (*Fig.* 136). But it must not be considered that when calcium is seen casting a shadow in the gall-bladder that the cystic duct will be occluded in all cases, for at the time of examination the obstruction may have been overcome by passage of the stone, by its slipping back into the gall-bladder, or by diminution of the inflammatory swelling in the region of the duct. Such factors make operative and post-mortem findings difficult to evaluate (*Figs.* 137–141).

Turning to the evidence obtained by cholecystography alone, it is a well-known finding that calcareous débris and calcification of the wall of the gall-bladder are, in almost every case, associated with non-filling of the gall-bladder following administration of the dye (*Figs.* 142, 143). In the 1932 series over 20 per cent of the stones visualized had calcium deposited in them, and in 22 per cent of cases the stones cast primary shadows and the gall-bladder was reported as non-functioning (*Fig.* 144). An example of calcification only on the gall-bladder side of the stone

FIG. 137.—Calcified stone in dye-filled gall-bladder. The interpretation placed on this is that the cystic duct previously blocked during the formation of the stone, has now become patent.
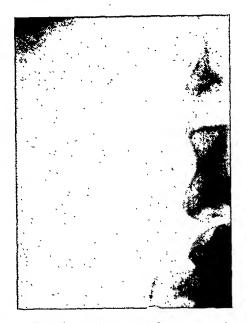
FIG. 138.—Another example of opaque stones in a dye-filled gall-bladder. Interpretation similar to *Fig.* 137. Note small size of stones, which on removal were only 1 mm. in diameter.
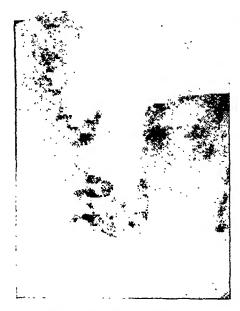
FIG. 139.—Interpretation : Gall-stones with radio-opaque centres formed when the cystic duct was occluded. Periphery of radiotranslucent material formed since cystic duct has become patent. Note dye in gall-bladder.

FIG. 140.—Interpretation : two radiotranslucent stones form the centre and are combined into one stone by calcified material in the gall-bladder, the cystic duct of which has again recently become patent as is shown by the presence of the dye.

FIG. 141.—Gall-stone indicating intermittent obstruction of the cystic duct and calcification alternating with deposition of cholesterol.
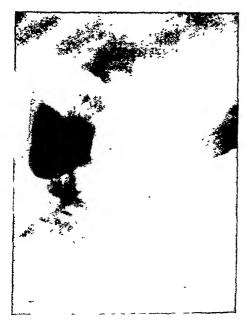
FIG. 142.—Calcareous débris at fundus of gall-bladder with ' fluid level '.   The shadow above this is not due to dye but is a primary shadow which did not increase on administering dye.

FIG. 143.—Gall-bladder with calcified walls. No dye entered it.

in the cystic duct is given in *Fig.* 145. In the normally-functioning gall-bladder with stones calcium deposition is comparatively rare.

It will be noted that judging from the size of the stones and the size and thickness of the calcified rings, one obtains the impression that the calcium deposition has occurred in all the stones at the same time and for the same length of time as the result of some sudden change in the biliary content from which, of course, the stones grow. An example, too, of primary calcium stones is given, and they will all be noted to be of the same size (*Figs.* 146, 147).

Andrews, Schoenheimer, and Hrdina[22] have shown fairly conclusively that cholesterol is deposited or crystallized out by withdrawal of the bile-salts from the gall-bladder contents. Normally in man the bile-salt cholesterol ratio is 20 to 1, and when the ratio falls below 13 to 1 cholesterol can no longer remain in solution (cholesterol is quite insoluble in water, and in the bile is dependent on the presence of bile-salts for its solution). Analyses of mixed gall-bladder bile in a post-mortem series of thirty stone-containing gall-bladders showed that the cholesterol content was 400 mgrm. and the bile-salt content 247 mgrm. per 100 c.c., or a bile-salt cholesterol ratio of 0·6. It will be noted that the cholesterol content is about normal and it is the bile-salt content which is markedly reduced.

While the normal bile-salt cholesterol ratio in man is perilously near the precipitation point, the ratio in animals is much higher and cholesterol stones are not normally found. In dogs the ratio is 100 to 1. Following Naunyn's[25] experiments Walsh and Ivy,[36] using dogs, and later Phemister, Day, and Hastings,[36] using rabbits, showed that human gall-stones may actually be absorbed if placed in the gall-bladders of those
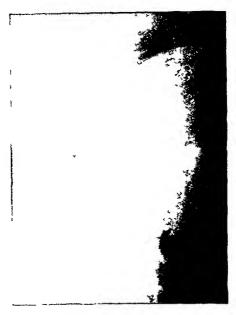
FIG 144 —Calcified stone in a gall-bladder in which there is no dye

animals. These experimental conclusions show the great importance of the rôle played by the bile-salts, and the value of those findings is enhanced by the work of Andrews, Schoenheimer, and Hrdina,[22] who found that in the infected gall-bladder bile-salts are absorbed rapidly and cholesterol very slowly if at all. This confirms the work of Neuman.[41] In the healthy gall-bladder, on the other hand, there is no differential absorption.

From the above evidence the following deductions can apparently be made. Under ordinary circumstances, with the cystic duct patent, gall-stones consisting mainly of cholesterol grow. But in order to grow the cholesterol stones must be constantly supplied with fresh bile entering by the cystic duct. Similarly, pigment stones grow by deposition of pigment from the bile, as is well seen in cases of hæmolytic jaundice. If the cystic duct is blocked it becomes evident that those

FIG. 145.—Gall-stones with no dye in gall-bladder and stone in cystic duct with calcification only on gall-bladder side. The interpretation given here is that the radiotranslucent centres were formed when the cystic duct was patent. The stone in the cystic duct now prevents any further cholesterol *from entering, and the calcium in the inflammatory exudate has become concentrated and deposited on* the stones. The upper margin of the stone in the cystic duct is not subjected to those changes and is not calcified.
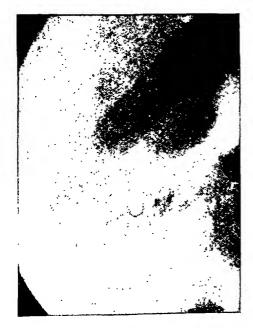
FIG. 146.—Calcium deposition on stones. Note that the size and thickness of the rings are approximately the same, indicating that calcification has occurred for the same length of time and at the same time in all the stones.

FIG. 147.—Primary calcium stones. Note that the stones are all of the same size. Some dye has entered the gall-bladder, indicating that the cystic duct is now patent.

stones must cease to grow, as it is rarely any longer considered that the wall of the gall-bladder secretes cholesterol—in fact the work of Andrews, Schoenheimer, and Hrdina[22] is quite against this view.

When the cystic duct has become blocked and there is associated chronic mild inflammation, there will be passed into the gall-bladder a steady stream of inflammatory exudate which contains calcium. If the gall-bladder cannot expand, as it frequently cannot do, because of the fibrosis of its walls, fluid must be absorbed and the calcium content will increase and precipitation occur on the stones or wall of the gall-bladders (*Fig.* 148). The photograph (*Fig.* 145) showing calcification only on the gall-bladder side of the stone would appear to be good evidence in favour of this view being correct. In a more or less healthy gall-bladder with
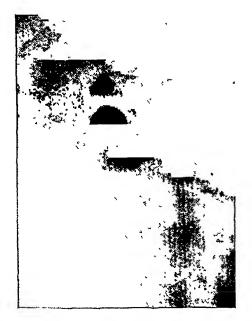
FIG. 148.—Calcified gall-stones. In the original film the outline of the gall-bladder can be easily seen without dye and this would indicate a high concentration of calcium in the fluid contents of the gall-bladder.

blockage of the cystic duct the viscus will expand to give the picture of hydrops and there will be no concentration of the calcium to any extent and therefore no deposition. If, on the other hand, the infection in the gall-bladder is acute and its duct is blocked, the condition of empyema will result. In fact when Andrews[42] examined the calcium content of the bile from acutely inflamed gall-bladders he found it to be low.

In an old untreated empyema of the chest calcification frequently occurs as a late process and is probably due to similar factors—namely, chronic inflammation acting in a cavity and leading to concentration of the inflammatory exudate poured in. If, on the other hand, the empyema is drained, and even although it keeps draining for years, calcification is rare because the inflammatory exudate is drained away and cannot be sufficiently concentrated to throw the calcium out of solution.

Similarly, calcification of an abscess rarely occurs if it is opened and drained, but may occur if no drainage is established.

It has been generally considered for a long time that while cholesterol stones are found unassociated with evidence of inflammation, calcium stones always indicate previous infection. The former statement is open to doubt, but the association between inflammation and calcium stones is admitted by all. It is precisely in those cases that blockage of the cystic duct is liable to occur.

IX. THE FREQUENCY OF CARCINOMA IN CASES WITH GALL-STONES

E. A. Graham[43] states that carcinoma of the gall-bladder constitutes 8 to 10 per cent of all cases of carcinoma in the female, and draws this conclusion from autopsy tables compiled by von Berencsy and von Wolff.[44] Graham[43] also states that from these tables it will be seen that carcinoma of the gall-bladder is three times as frequent as carcinoma of the lip, about twice as frequent as carcinoma of the rectum, of about the same frequency as carcinoma of the breast, and a little less than half as frequent as carcinoma of the stomach. *From the above figures Graham concludes that the operative risk of removal of gall-stones is much less than the risk of the patient developing carcinoma of the gall-bladder.*

Lentze[45] found in female patients over 39 years of age who had gall-stones that there was associated carcinoma in 5·1 per cent of cases. Rolleston[28] states that 4·5 per cent of all cases of cholelithiasis are accompanied by carcinoma. Moynihan[46] gives 5 per cent, Riedel[47] 7 to 8 per cent, Mayo-Robson[48] 10 per cent, Schröder[49] 14 per cent, and Graham[43] himself 8·5 per cent of all cases, and later states that " it would seem reasonable to conclude, however, that at least 4 or 5 per cent of all women in the cancer age who have gall-stones will develop carcinoma of the gall-bladder, and perhaps further study will show that it may actually be much higher."

These figures are indeed alarming and would mean that when gall-stones are recognized by the radiologist one out of every ten to twenty cases had carcinoma of the gall-bladder. It would be a serious error for the radiologist to miss one single case of gall-stones, for obviously all gall-bladders with stones would require to be removed *immediately* by operation.

In the 22,365 operations on the biliary tract at the Mayo Clinic, Judd and Gray[23] found stones in 15,422 cases and carcinoma of the gall-bladder in 212 cases, giving an incidence of malignancy of 1·3 per cent *in all cases of gall-stones operated on.* But they also state that in all cases in which the possibility of carcinoma was suspected operation was performed, but not all cases of gall-stones were operated on, so that the percentage should possibly be still lower.

In the cholecystographic data for 1932, stones were found at operation in 415 cases. Of these there were 2 cases of carcinoma of the gall-bladder, giving an incidence of 0·48 per cent.

Leitch[50] states that the lowest incidence reported is that of Candler,[51] who found, in post-mortem statistics from an asylum practice, an incidence of only 2 cases of carcinoma in 315 cases of calculi (0·6 per cent).

It seems difficult to believe that carcinoma of the gall-bladder is three times as frequent as carcinoma of the lip and of about the same frequency as carcinoma

of the breast. If these statements were true, surely carcinoma of the gall-bladder would be found far more frequently. Probably the explanation of the statements of Graham[43] is to be found in the fact that they are based on post-mortem statistics, which have frequently been shown to be highly unreliable. Operation statistics ought to be better, but probably the best figures will ultimately be obtained from the study of cholecystographic data and their correlation with operative findings. So far as the above radiological evidence goes, it does not support such a high incidence and is more in keeping with what one would expect on broad consideration of the subject.

Finally, it must not be concluded that the view is taken that gall-stones do not produce cancer, for it would seem that most of the evidence is in favour of this theory and most cases of carcinoma of the gall-bladder are accompanied by stones.

SUMMARY AND CONCLUSIONS

1. A standard method of roentgenological reporting of cholecystograms has been given.

2. The technique of administration of the dye as followed at the Mayo Clinic has been outlined, and it would appear that the oral technique, if carefully carried out as suggested, is just as accurate as the best results obtained by the intravenous method of administration.

3. The cholecystographic data for 1932, consisting of 732 cholecystograms all checked by operation, have been analysed and the accuracy obtained in the various groups expressed. The interpretation of the terms 'poorly-functioning' and 'non-functioning' in terms of pathology has been given. Various possible errors in interpretation have been pointed out.

4. The roentgenological basis of the diagnosis of tumours, both simple and malignant, has been discussed and the differential diagnosis given.

5. Peptic ulcer of the stomach and duodenum has been shown to play no apparent part in interfering with the filling of the gall-bladder.

6. The importance of realizing that a good cholecystogram does not rule out even extensive and serious disease of the liver has been demonstrated.

7. Delayed emptying of the gall-bladder should not be regarded as evidence of disease.

8. Deposition of calcium in the gall-bladder is evidence of the fact that at the time of its deposition the cystic duct was blocked, but it must also be noted that calcium deposit does not always indicate that the cystic duct is blocked at the time of examination, as patency of its lumen may have been restored. If the above suggestion is accepted it would indicate that calcified gall-stones form a greater indication for operation than those which are not calcified.

9. From the evidence obtained the suggestion is put forward that gall-stones are accompanied by carcinoma of the gall-bladder in probably less than 1 per cent of cases.

In conclusion, I wish to state that much of the material in this paper concerning (1) technique, (2) statistical review of cholecystographic data, and (3) the important points in the diagnosis of tumours of the gall-bladder, was obtained from perusal of articles written by Dr. B. R. Kirklin, but I think I am justified in quoting them in full rather than only giving references, as his work is not so well known in Britain as in America.

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AN UNUSUAL TUMOUR OF THE NECK

By R. E. NORRISH

SURGICAL REGISTRAR, ROYAL NORTHERN HOSPITAL

THE uncommon features presented by a solid tumour removed from the lateral aspect of the neck are believed to be of sufficient interest to warrant the placing of the following case on record.

The patient was a man, aged 62 years, who came to the hospital complaining of a swelling behind the angle of his lower jaw. He first noticed it five years previously; it was painless and was gradually increasing in size.

A movable tumour was present, in size a little smaller than a hen's egg. It was firm in consistency, non-fluctuant, and there was no evident fixation to adjacent structures. Under general anæsthesia the tumour was exposed through a transverse incision. It lay beneath the deep cervical fascia, projecting forward from under cover of the sternomastoid, and extending upwards as far as the lower pole of the parotid gland. (No definite attachment, however, to the latter was demonstrated.) It was easily enucleated from its surrounding capsule. The specimen obtained was ovoid in form, and covered by a thin membrane in which a number of blood-vessels were to be seen. Its cut surface was greyish-yellow in colour, with one or two small areas of softening. Microscopically (*Figs.* 149, 150) there were evident a large number of alveoli, most of them small in size, but a few almost reached the size of small cysts. Each was lined by a well-marked epithelium of very uniform type throughout the section. This was constituted by a double layer of cells, the inner being columnar in form, and the outer cuboidal. Here and there the epithelium projected into the alveoli, forming processes which occasionally showed branching. The cells were non-ciliated. Surrounding these alveoli and extending between them was lymphoid tissue, densely packed and with germinal centres, and around the whole a fibrous capsule was evident. No muscle or cartilage was found in the sections, and no sebaceous gland, hair follicle, or Hassal formations were seen.

In 1898, Neisse[1] described the inclusion of parotid tubules in lymphatic glands. The developing salivary buds are at an early stage surrounded by a diffuse mass of lymphoid tissue which gradually becomes collected into nodes, and around these, capsules are eventually formed. During this process certain salivary epithelial tubules may become separated and included within the lymphatic gland. These formations were demonstrated by Neisse in many newly-born infants, and they have also been shown in association with the submaxillary salivary gland. It is from these remnants that a tumour is believed occasionally to arise.

During the past twenty-five years there have been described a number of cases bearing a close resemblance to each other. Two cases were described by Albrecht and Artz,[2] who pointed out the striking resemblance of the included epithelium to that of salivary duct. This view is endorsed by G. W. Nicholson,[3] who presents two more examples. Ten cases are reviewed by Moatti,[4] and this writer points

out that all have certain properties in common : the swellings are all situated either within the parotid gland or just below it, behind the angle of the jaw, are encapsulated beneath the deep cervical fascia, and are easily enucleated.   Histologically they all

FIG. 149.—Section of tumour removed (low power).

FIG. 150.—Section of tumour removed (high power).

show alveolar formation surrounded by lymphoid tissue with well-marked germinal centres.   The alveoli usually have a double epithelial layer, the inner being columnar. Some of the alveoli are large and form cystic spaces, into which papillary processes may project.

The case described above is in accord with almost all these features, though the lymphoid tissue is in places rather sparse and seems to be crowded out by the large number of alveoli.

The precise origin of these swellings is undecided. On histological grounds Nicholson believes that they are adenomata of salivary origin contained within lymphatic glands, and he calls them ' adenomata of præ-parotid glands '. This view has received considerable support, and the term ' lympho-glandular cystoma ' is mentioned by certain writers.

It is, though, difficult to deny the possibility of a branchial origin to these tumours, for they occur in the region of the neck where branchial remnants are so commonly found. They contain elements which are found in branchial derivatives, and the association of lymphoid tissue with pharyngeal outgrowth is well known. In the entodermal type of branchial cyst it is not uncommon to find occasional Hassal's corpuscles, small amounts of cartilage, or striped muscle. It is noteworthy that these structures have not been mentioned in the small series of cases quoted above, and certainly none was evident in the sections of the tumour removed in the case described. The occurrence, too, of columnar epithelium in a tumour so near the surface, is unusual in a branchial cyst, for this is essentially the situation of the more usual variety with its stratified squamous epithelium (Hamilton Bailey[5]).

These considerations lend weight to the suggestion that the tumours are not of branchial derivation, and their origin from salivary remnants is more probable.

I am indebted to Mr. L. E. Barrington-Ward for permission to publish this case, and to Dr. A. H. Robb-Smith and Dr. P. O. Ellison for their assistance with the histology of the tumour.

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EXPERIMENTAL SURGERY

PATHOLOGICAL CHANGES INDUCED IN THE MAMMA BY ŒSTROGENIC COMPOUNDS

By HAROLD BURROWS, C.B.E.

RESEARCH INSTITUTE, THE CANCER HOSPITAL (FREE), LONDON.

(Being a Hunterian Lecture delivered at the Royal College of Surgeons of England on January 14th, 1935)

THE regulation of the structure and function of the mamma by hormones elaborated in other organs of the body has long been recognized. Thirty years ago Halban showed ground for supposing that the increase of the breast at puberty was secondary to the awakened activity of the ovary at this period, and that the enlargement of the mamma in pregnant women and in newly born babies of either sex was caused by some substance derived from the placenta. His conclusions have been established by subsequent experimental inquiry.

KETOHYDROXYŒSTRIN   KETOMETHOXYŒSTRIN   TRIHYDROXYŒSTRIN

EQUILENIN   DIHYDROXYŒSTRIN   9:10-DIHYDROXY-9:10-DI-*n*-PROPYL-9:10-DIHYDRO-1:2:5:6-DIBENZANTHRACENE

FIG. 151.—Structural formulæ of œstrin and some allied œstrogenic compounds.

Investigations in the laboratory have shown that mammary changes are brought about by hormones derived from the ovarian follicles and placenta, and perhaps from other sources. These hormones belong to a group of chemical compounds which exercise a remarkable influence on certain organs in the body, especially those concerned with reproduction, both in the male and in the female. *Fig.* 151 displays the structural formulæ of some of the œstrogenic substances the biological properties of which have been under examination in our laboratories. It will be seen that they have a general similarity of structure. They may be referred

to collectively as ' œstrogens ', because they all produce in mice and rats those changes in the vagina which are associated with œstrus in these animals, and which, with ease and certainty, can be recognized by the microscopical examination of smears taken from the vagina at successive intervals of time.

Of these œstrogens the best known is ketohydroxyœstrin or œstrin, with which the greater part of the present paper will be concerned. The recognized *changes induced in the female mamma by amounts of œstrin which are not* excessive or too long continued—that is to say, the physiological effects—are an increase of the fat-containing stroma, with proliferation and dilatation of the ducts. In mice œstrin appears to have little or no direct influence in the induction of lactation, this being dependent upon hormones derived from the corpus luteum, the anterior hypophysis, and possibly elsewhere. The normal function of œstrin, so far as concerns the mamma of the female mouse, appears to be confined to a preparation of this organ, so that lactation subsequently may be brought about by the action of other hormones. No further reference will be made now to what may be regarded as the physiological functions of œstrin, our present purpose being to consider the part which this hormone can play in the causation of pathological lesions of the breast. The experimental investigations of various inquirers on this subject fall into two distinct groups, according to whether the tests were made with purified œstrin or not.

Before 1929, in which year Doisy, Veler, and Thayer, and also Butenandt, showed how œstrin might be separated in a crystalline form from the urine of pregnant women, all experimental work in this field was carried out under a great disadvantage. The methods used, apart from mere observation of the course of nature, consisted of the removal or insertion of whole tissues, or the injection of crude extracts made from them. *In such circumstances any results obtained could not be attributed with confidence to the presence or absence, excess or deficiency, of any one particular chemical substance. Some valuable knowledge was* obtained by these indirect means, and it will be convenient, without presenting a complete historical review, to recall one or two of the conclusions reached, before considering the more exact data acquired by experimentation with œstrogens in a chemically pure state.

I. EXPERIMENTS MADE BEFORE THE ISOLATION OF ŒSTRIN

In 1916 Lathrop and Leo Loeb, using female mice of several different strains, some of the strains having a higher incidence of spontaneous mammary cancer than others, found that removal of the ovaries, if carried out before the age of 6 months, led to a pronounced *decrease in the incidence of cancer* of the breast in these animals, although it did not entirely prevent it. Furthermore, in the few cases in which cancer arose in castrated female mice, it appeared later in life than in non-castrated mice of the same strain. Castration of mice above the age of 6 months did not have any pronounced effect in preventing mammary cancer. Continuing these observations, Loeb published a second paper in 1919 which threw further light on the connection between ovarian activity and cancer of the breast, for he was able to show, with greater precision than before, a contrast between the results following early and late castration respectively. If the ovaries were removed from mice between the ages of 3 months and 5 months, cancer of

the mamma was almost entirely prevented. If the castration was done between the fifth and the seventh month, the cancer rate was diminished, and when cancer did appear it was at a later age on the average than in non-castrated mice. Removal of the ovaries after the eighth month of life had no effect in reducing the incidence of mammary cancer.

Cori followed up Loeb's investigations. He removed the ovaries from mice belonging to a strain in which 78 per cent of the females suffered from spontaneous mammary carcinoma. In 49 of these mice which had been castrated at ages varying from 2 to 6 months, and which lived to 19 months or more, mammary cancer developed in 5 only. The incidence of cancer in these mice was thus reduced, by castration in the first six months of life, from 78 per cent to 10 per cent. In a second series he castrated 100 mice belonging to the same strain just after weaning—that is to say, when they were between 15 and 22 days old. At the end of 10 months 86 were still alive, and 60 reached the age of 20 months. Not one of them suffered from mammary cancer; whereas at 20 months of age, tumours had appeared in 74 per cent of the untreated control mice belonging to the same strain.

W. S. Murray, in addition to confirming the effect of early castration in preventing mammary cancers in female mice, carried out some further experiments which might be regarded as the reverse of those of Loeb and Cori. He used a strain of mice among which 80 per cent of the untreated females eventually suffered from mammary carcinoma. Tumours of the mamma did not appear in the untreated breeding males of this stock. He castrated 210 mice of each sex belonging to this strain, when they were between 4 and 6 weeks old, and transplanted subcutaneously in the abdominal region of each male an entire ovary taken from a sister. His results are shown in *Table I*.

Table I.—THE EFFECT OF CASTRATION ON THE INCIDENCE OF CANCER OF THE BREAST IN MICE
(*W. S. Murray*)

	NUMBER OBSERVED	NUMBER IN WHICH CANCER OF BREAST OCCURRED	PERCENTAGE	MEAN AGE AT WHICH THE TUMOURS APPEARED
				Months
Untreated breeding females ..	479	367	80	10·5
Spayed females	210	36	17·1	17·5
Castrated males with ovarian transplants ..	210	15	7	14·4
Castrated males without ovarian transplants ..	241	0	0	–

Goormaghtigh and Amerlinck treated doe mice with daily subcutaneous injections of an œstrin-containing extract prepared, they state, according to the method used at that time by Zondek and Aschheim, and by Laqueur. The administration was continued for several months, each dose containing 6 rat units

of œstrogen. The usual change caused in the mamma by this treatment was a dilatation of the ducts and acini, which became very abundant. In some of the cystic dilatations the epithelium was atrophied; more often it showed proliferation, the ducts being sometimes converted into solid cords. Infiltration with leucocytes was not uncommon. The authors attribute both the epithelial proliferation and the presence of leucocytes in large part, though not entirely, to the retention of secretion. In some examples there was a proliferation of the ducts without dilatation; in these instances mitoses were abundant in the epithelium and the nuclei varied greatly in size. It was particularly noted that the changes produced by these extracts were not equally distributed throughout the mammæ; one part of a gland might appear normal, or nearly so, while another part showed pronounced alteration. Occasionally adenomatous formations developed and were visible to the naked eye, and in one case an encephaloid carcinoma arose.

II. EXPERIMENTS WITH ŒSTROGENS IN A CHEMICALLY PURE FORM

The results of the foregoing experiments are, on the whole, in accord with those obtained by more recent and exact investigations carried out with œstrin itself in an uncontaminated state. Lacassagne's work calls for particular recognition in this field. In an early experiment he gave weekly injections of crystalline benzoate of œstrin dissolved in sesame oil to 5 young mice, commencing when they were between 10 and 18 days old. Of these mice 3 were males and 2 were females. They belonged to a strain in which about 72 per cent of the untreated females eventually suffered from spontaneous mammary carcinoma, though none of the males belonging to this strain had been known to be thus affected. In every one of the 3 males treated by œstrin in this experiment cancer of the breast developed within six months, one of the mice having two separate tumours. Mammary cancer appeared also in one of the two females, at the early age of 4 months.

Additional results of a similar kind have been reported by Lacassagne in a second paper. In the same manner as before he administered œstrin to mice belonging to two different strains to which I shall refer as Strain A and Strain B. The untreated females of Strain A show an incidence of mammary carcinoma of 72 per cent, while only 2 per cent of the untreated females of Strain B suffer in this manner. Weekly injections of œstrin into mice of Strain A resulted in the appearance of mammary carcinoma in every one of 5 males so treated, and of one tumour in 7 females. With mice of Strain B, after a similar course of treatment, 2 among 8 males and 1 among 7 females eventually suffered from malignant mammary tumours; and the carcinomata appeared in this group of mice at a more advanced age than that at which it arose in mice belonging to Strain A. In yet another strain of mice treated with œstrin in the same way as those just mentioned, no mammary tumours developed. Lacassagne made the further interesting discovery that in mice of Strain A—that is to say, the mice among which spontaneous cancer of the breast was frequent among the untreated females—the œstrous cycle was regular, lasting five days, œstrus proper occupying about forty-eight hours. In Strain B, on the other hand, great variations in the cycle were noticed; œstrus was of short duration, occurred at irregular intervals, and was apt to pass unperceived, and diœstrus often lasted a week. It was observed also that an

injection of œstrin caused a rapid and prolonged œstral reaction of the vagina in mice of Strain A and only a fugitive response in those of Strain B. These facts, showing a contrast between the two strains in their reaction to œstrin, suggested to Lacassagne that the difference of cancer incidence in the two groups might be referred possibly to this difference of sensitivity toward the action of œstrin.

Another observer, Harde, also has noticed an unusually long period of œstrus in two strains of mice in which mammary carcinoma is very common, and she states that exaggerated œstrus sometimes can be detected in mice carrying spontaneous mammary tumours.

Geschickter, Lewis, and Hartman administered repeated doses of œstrin to male monkeys and compared the mammary condition, as shown by material removed at a biopsy before the administration, with that found at the end of the experiment. They used 2 *Cebus* monkeys which were treated by subcutaneous doses of 500 rat units of œstrin (amniotin) for a period of ten days, and 5 *Macacus* monkeys which were treated in the same way for six weeks with smaller daily doses, the amounts of which are not clearly stated in their paper. Though the consequences were most pronounced in the latter series they were alike in character in all the 7 individuals. The mammæ were enlarged, and showed, when examined microscopically, an increase in length and dilatation of the ducts, an increase in the number of layers of epithelial cells lining them, and a proliferation of the periductal connective tissue. In other words, the monkeys all presented the appearances typical of cystic mastopathy, or, as it used to be called, ' chronic cystic mastitis '.

During the last two years experiments have been in progress at the Research Institute of the Cancer Hospital, with the object of elucidating the effects of œstrin when persistently administered over long periods of time. For an ample supply of pure œstrin we are indebted to the very great generosity of Dr. Girard.

The results about to be described are based on the microscopical examination of 312 mammæ taken from 199 mice, of which 28 were females and 171 were males. Of the 199 mice used, 130 had been treated with œstrin or some allied compound during a period of fifty days or more, and 69, including 53 males, were controls. Among the controls were 30 males which had received applications of benzene free from œstrogen in just the same manner as those treated with benzene in which some œstrogen was dissolved. The remainder of the male control mice had received either no treatment (13) or were mice which had been used for grafting with tumours (10).

The method used in the greater part of this work has been to apply œstrin, dissolved in benzene so as to make a 0·01 per cent solution, to the non-epilated skin of the mouse's back, in the interscapular region, by a single application of a small paint brush. These applications were made twice a week, and were continued usually until the death of the animal.

ANATOMICAL CONSIDERATIONS

The female mouse, though subject to individual variations, normally has five mammæ on each side. These are far less discrete and clearly circumscribed than is the human mamma, and, when fully developed, they extend over a large proportion of the subcutaneous layer of the animal's body. The most conspicuous nipple is the fourth, counting from before backwards, and is situated in the iliac

region. About $4\frac{1}{2}$ mm. forwards and in a dorsal direction from this nipple, and surrounded by mammary tissue, is a lymphatic gland. This iliac lymphatic gland is almost constantly present in mice, and I have used it as a landmark for the mamma in both males and females. In every case a strip of skin and subcutaneous tissue has been taken, including this iliac lymphatic gland and the readily seen blood-vessels which lead from it towards the lumbar region. These blood-vessels are surrounded by a mass of fat which, in the female mouse, and sometimes in the male, contains mammary ducts and acini. No microscope section in which the iliac lymph-gland is not displayed has been used for statistical purposes in the present inquiry. *Fig.* 152 represents a section made in the way just described through the iliac lymphatic gland of an unmated doe, and shows the distribution of mammary ducts around the gland. *Fig.* 153 is a photograph of a similar section taken from a mouse which had recently littered. These illustrations are intended to justify, if possible, the selection of the iliac gland as a landmark for the mamma. And here an explanation will be necessary. The majority of our experiments have been carried out on male mice; and although the mamma of the male is in some respects more suitable than that of the female for studying the effects of œstrogens, yet in the mouse there is one serious disadvantage—namely, the absence from the male of any nipple, areola, or other external sign to mark where the mammary rudiments are to be found. The iliac lymph-gland, therefore, was chosen as a landmark merely because no better one was discovered. The only alternative seemed to be the making of serial sections in every case, and this was not practicable. Some justification for the choice of the iliac gland as a landmark is required, because microscopical sections prepared in this way from normal untreated male mice only occasionally show any mammary tissue at all; and in the exceptional instances where mammary tissue is present it is extremely scanty. The mamma of the normal untreated male mouse consists only of a few very small vestigial ducts which are invisible to the naked eye (*Fig.* 154).

FIG. 152.—Section through fourth mamma of an old untreated, unmated female mouse. L. Iliac lymph-gland; M, Mammary ducts; S, Skin. (× 12).

Similar sections made from male mice which have been treated for a sufficient period with œstrin more often reveal mammary tissue, sometimes in abundance.

On the average about twenty sections of each mamma were examined, and if any one of these sections from a male mouse showed the presence of a duct, the result was recorded as positive. In some mice both iliac mammæ were examined, and in others only one. Among the treated mice it happened not infrequently that a pronounced development of mammary tissue might be seen in one of the mammary regions, while sections made from its fellow of the opposite side revealed no mammary tissue at all. Possibly in such instances no mammary vestige was present on that side, for anatomical variations occur, and one of the nipples and mammæ may be absent even in the female mouse. Probably also the iliac

lymph-gland has not an unvarying relationship with the nipple and vestigial mamma ; and it is conceivable, too, that an extension of the vestigial ducts under the influence of œstrin might take some other direction than towards the iliac lymph-node.

In spite of the anatomical disadvantages entailed by using the iliac lymph-gland as a landmark for the mamma, the results of the method have been satisfactory from the practical standpoint.
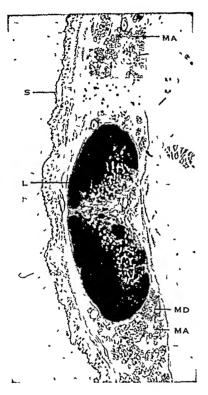
FIG 153 —Section through fourth mamma of a mouse which had recently littered. Shows large number of mammary ducts and alveoli surrounding the iliac lymph-gland S Skin, L, Lymph-gland, MD, Mammary ducts (dilated), MA, Alveoli (× 12)

FIG 154—Section through the iliac lymph-gland of an untreated male mouse taken in a similar manner to those shown in *Figs* 152, 153 L, Lymph-gland , VM, Vestigial mamma No mammary vestiges are present outside the circle (× 12)

The effects of œstrogenic compounds upon the mammæ of male mice, as seen in microscopical sections, may be considered under the following headings :—

1. Proliferation of ducts (gynæcomastia)		4. Leucocytic infiltration
2. Dilatation of ducts	Cystic mastopathy	5. Increase of periductal fibrous tissue
3 Hyperplasia of duct epithelium		6. Alveolar formations (adenomata ?)
		7. Cancer

1. Proliferation of Ducts or Gynæcomastia.—Sections of 29 mammæ taken from 23 adult male mice of various ages which had not been treated with benzene or any œstrogenic compound, revealed the presence of mammary ducts

in 5 only, and in these but a few cross-sections of ducts were seen (*Table II*). In 57 mammæ from male mice which had received applications of benzene only to the skin for prolonged periods, mammary ducts were seen in 12, and in 4 of these more than ten cross-sections of ducts were counted. In every instance the ducts were vestigial in character (*Fig. 155*). In 97 mammæ taken from male mice which

FIG. 155.—Section through duct (MD), of vestigial mamma of untreated male mouse (× 180)

had been treated with œstrin for a period of more than fifty days, ducts were visible in 62, and in 56 of these more than ten ducts could be seen in single sections. In 77 mammæ from male mice treated with œstrogenic compounds other than

Table II.—Proliferation of Mammary Ducts in Male Mice Following Treatment with Œstrogens for more than Fifty Days

TREATMENT	NUMBER OF MAMMÆ EXAMINED	NUMBER SHOWING DUCTS	PERCENTAGE	NUMBER SHOWING MORE THAN 10 DUCTS IN A SECTION (GYNÆCOMASTIA)	PERCENTAGE
Controls. No drugs applied	29	5	17 2	0	0
Benzene only ..	57	12	21 0	4	7 0
Œstrin in benzene	97	62	63 9	56	57 2
Other œstrogens ..	77	36	46 7	25	32 4

œstrin, mammary ducts were found in 36, with evidence of their proliferation in 25 (*Table II*). My intention had been to count the ducts shown in the different series of sections for comparison, but this was found impracticable owing to the great number of ducts present in some of the mice which had been treated with

œstrogenic compounds. However, an estimate of numerical value has been obtained by separating cases into two categories according to whether more than ten or less than ten ducts are visible in a single microscopical specimen. In making these records only those particular sections which showed the maximum number of ducts were used. Thus, in a series of sections made from an untreated male mouse the majority might show no mammary tissue at all, a single duct appearing in but a few sections; such a case would be recorded as positive in *Table II*. In the same way, if some preparations displayed only five or seven ducts, for example, while others from the same mamma showed more than ten, the record was based on the latter.

FIG. 156.—Mamma of a male mouse treated with œstrin for 190 days. Illustrates gynæcomastia. S Skin; L, Lymph-gland; MD, Dilated mammary ducts. (× 12)

Seeing that more than ten ducts were rarely seen in sections of mammæ taken from male mice which had not been treated with any œstrogenic compound, whereas sections taken in a similar manner from untreated female mice nearly always showed more than ten ducts, it seems justifiable to apply the term ' gynæcomastia' to the proliferation of ducts induced by œstrogenic substances in the mammæ of male mice, and revealed by this numerical criterion.
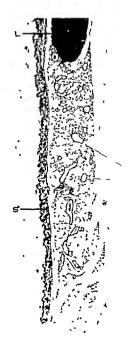
Another justification for using the term ' gynæcomastia' in the present circumstances is the apparent correspondence, within limits, between the changes induced by œstrin in the mamma of mice and pathological lesions of a comparable nature which occur in man.

2. Dilatation of the Ducts.—This was never seen in untreated male mice. In those which had
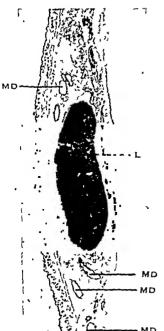
FIG. 157.—Mamma of male mouse treated with œstrin for 245 days. Shows gynæcomastia. S, Skin; L, Lymph-gland; MD, Dilated mammary ducts. (× 12.)

been subjected to œstrin, dilated ducts were present in 52 mammæ out of a total of 58 in which mammary ducts could be demonstrated (*Figs.* 156–158). The cystic dilatations are filled with a material which stains pink with eosin and appears homogeneous. The cysts themselves seem to be formed,

in part at least, through a general increase in the length and diameter of a duct causing tortuosity and perhaps kinking.

The ducts may be lined by a cuboidal or columnar epithelium (*Fig.* 159) or by flattened epithelium (*Fig.* 160). These illustrations exemplify the fact that the type of epithelium does not depend upon the degree of tension within the duct. In *Fig.* 160 the duct appears flaccid, though lined by a flattened epithelium, whereas in the well-distended duct of *Fig.* 159 the epithelium varies from cuboidal to columnar.

FIG. 158 —Mamma of a male mouse treated with œstrin since birth (279 days). Illustrates cystic mastopathy. S, Skin; L, Lymph-gland; MD, Dilated mammary ducts. Hyperplasia of duct epithelium is present, though not distinguishable under this magnification (× 12.)

In untreated unmated adult female mice, very wide differences are to be seen both as regards the number of mammary ducts present and their calibre. Such differences depend to some extent upon the stage of the œstrous cycle at which the mouse was killed. During œstrus the mammary ducts in mice become dilated, and, normally, return to their former thread-like dimensions during metœstrus (Cole). But this contraction is not always complete, and dilated ducts often

FIG. 159.—Mamma of male mouse treated with œstrin for 133 days. S, Skin; L, Iliac lymph-gland; BV, Blood-vessel. Three dilated ducts are shown. They are lined by a single layer of cells, varying from cuboidal to columnar, and are filled with material staining pink with eosin. Note absence of peri-ductal fibrosis or inflammatory reaction. (× 56.)

may be found in untreated female mice at all stages of the œstrous cycle. Among elderly unmated and untreated female mice great contrasts exist. In one the mammæ may be represented by a few non-dilated ducts resembling in their form the vestigial ducts seen in the untreated male, while in another the ducts are numerous, more dilated, and show here and there varying degrees of epithelial hyperplasia.
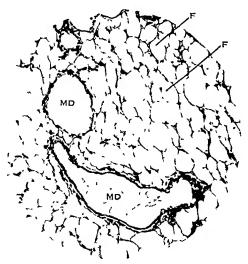
FIG. 160.—Mamma of male mouse treated with œstrin for 245 days. F, Fat cells; MD, Mammary ducts. Note: (a) Flaccid appearance of ducts, (b) Flattened epithelium lining the duct; (c) Absence of periductal fibrosis and inflammatory reaction. (× 100.)

3. **Hyperplasia of the Epithelium.**—This, like dilatation of the ducts, was never seen in the mamma of an untreated male mouse, though present in 40 per cent of the animals which had been submitted to prolonged treatment with œstrin (*Figs.* 161–164). Epithelial hyperplasia was of less frequent occurrence than dilatation of the ducts, and ensued later in the course of treatment with œstrin. A diagnosis of cystic mastopathy has been made in the course of this investigation only when dilatation of ducts and epithelial hyperplasia have both been present. The two conditions do not appear to advance at an equal rate as the experiment proceeds, and on looking through a number of microscope specimens the impression is acquired that to some extent the two conditions may be in inverse relationship—that is to say, that epithelial hyperplasia seems more often pronounced in those specimens which show relatively little dilatation of the ducts, while in the presence of extensive dilatation of ducts there may be but little hyperplasia of the epithelium.

If a wider experience substantiates this observation, it may be necessary to modify somewhat our views of the prognostic significance in women of mammary cysts. They might be regarded as sinister as they indicate an excess of œstrogenic effect—an excess which, if it continues, is known to lead eventually to epithelial hyperplasia. This latter, representing as it does a more advanced stage in the pathological process, would give rise to a more acute apprehension of the supervention of cancer. Naturally, because more easily observed, the cysts have hitherto
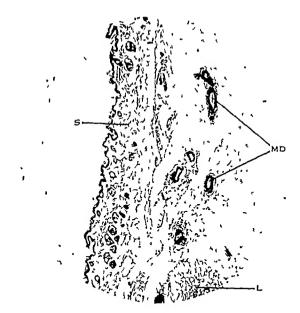
FIG 161 —Mammary tissue of male mouse treated with œstrin for 142 days   Shows hyperplasia of epithelium of mammary ducts (MD) without dilatation   S, Skin , L, Lymph-gland   (× 56)
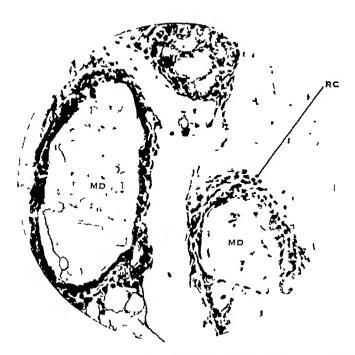
FIG 162 —Mammary tissue of male mouse treated with œstrin for 154 days.   Shows hyperplasia with dilatation of mammary ducts (MD)   There is some round-cell infiltration (RC), and a few leucocytes are seen within the lumina of the ducts   (× 145)

FIG. 163.—Section through two mammary ducts of a male mouse treated with œstrin for 144 days. Note : (*a*) Hyperplasia of epithelium with but little dilatation of duct ; (*b*) Absence of periductal fibrosis ; (*c*) Absence of inflammatory reaction. (× 400.)

FIG. 164.—Section through wall of dilated mammary duct in a male mouse treated with ketomethoxy-œstrin for 337 days. Shows the partial replacement of hyperplastic cells (Hy) by anaplastic epithelium (An). (× 500.)
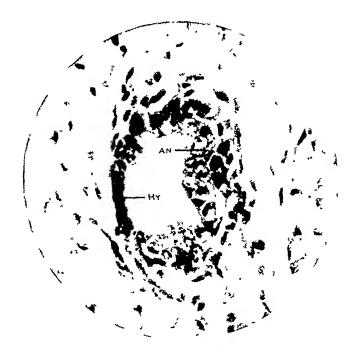
FIG. 165 —Section through mammary duct of a female mouse treated with ketomethoxyœstrin for 349 days.   Shows the partial replacement of hyperplastic epithelium (Hy) by anaplastic epithelium (An). (× 500)
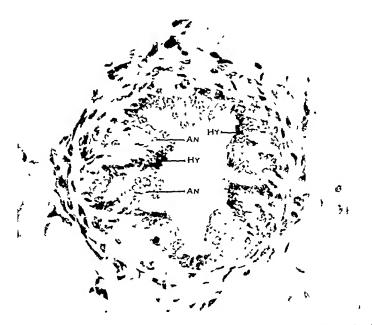
FIG 166 —Section through mammary duct of a female mouse treated with œstrin for 429 days. Shows the partial replacement of hyperplastic epithelium (Hy) by anaplastic epithelium (An). (× 400)

attracted too much attention, it would seem, in comparison with the more ominous hyperplasia, which has received, perhaps, too little. This is unfortunate, seeing that advanced hyperplasia may exist in one part of a breast with slight, if any, dilatation of the ducts, while in another part of the same breast there may be conspicuous cysts without overgrowth of the epithelium.

In our experimental work sections of mammæ have been regarded as showing epithelial hyperplasia when some of the ducts possess a lining more than one cell in thickness. In the earlier stages of this hyperplasia the cells have relatively little protoplasm and their nuclei stain darkly. After the applications of œstrin have been continued for a year or so a change may be seen not infrequently in certain areas of such hyperplastic epithelium (*Figs.* 164–166).

FIG. 167.—Section through two mammary ducts of a male mouse treated with œstrin for 234 days. There is copious round-cell infiltration. (× 180.)

The change consists in the appearance at various foci of larger cells, containing faintly staining cytoplasm with large, pale, vesicular nuclei and large nucleoli. These anaplastic-looking cells multiply and form small masses which replace the pre-existing type of epithelial cell.

4. Leucocytic Infiltration.—Leucocytic infiltration around the ducts is occasionally seen (*Figs.* 162, 167). The majority of the invading cells have the appearance of lymphocytes. As the condition is largely a matter of degree and may affect some of the ducts only, while others in the same microscopical section may be free, the relative frequency of leucocytic infiltration has not been expressed in numerical terms.

5. Increase in Periductal Fibrous Tissue.—Regarding the frequency with which an increase of the connective-tissue stroma surrounding the mammary ducts may occur under the influence of œstrin, it is also difficult to speak with

confidence. There is little tendency in the mouse, as compared with man, toward the formation of fibrous tissue, and I should prefer to leave as an open
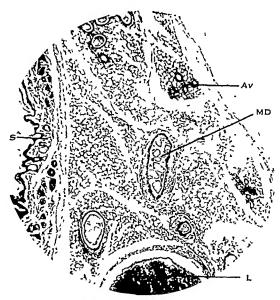
FIG. 168.—Mamma of castrated male mouse treated with œstrin for 411 days.   S, Skin ; L, Lymphatic gland ;   MD, Mammary duct ,   Av, Alveolar formation (? adenoma).   Note :   (a) Periductal fibrosis ; (b) Hyperplasia of duct epithelium.   (× 56)
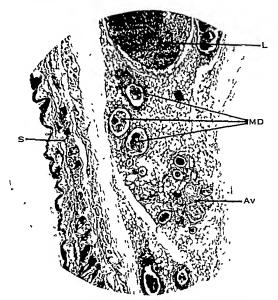
FIG. 169.—Mamma of castrated male mouse treated with œstrin for 419 days.   S, Skin ;   L. Lymphatic gland ,   MD, Mammary ducts ;   Av, Alveolar formation (adenoma ?).   Periductal fibrosis and epithelial hyperplasia are present.   (× 56)

question the frequency with which an increase of the periductal stroma may take place as a consequence of the administration of œstrin to mice. Occasionally

the increase of periductal fibrous tissue is considerable and easy to recognize (*Figs.* 168, 169).

Before discussing the development of tumours, a few words may be said about the distribution of the foregoing changes effected in the mamma by œstrin. The treatment of mice with œstrogenic compounds does not appear to affect the whole of a mamma in an equal degree. A similar observation has been made in connection with the effects of œstrogens on the prostate (Burrows). Even where obvious changes are present throughout all the mammary tissue visible in a single section, the nature of the lesions often varies in character and degree in different microscopic fields, or even in different parts of the same field. Dilatation may be more pronounced in one group of ducts than in another; epithelial hyperplasia may be advanced in one group of ducts whether cystic or not, and absent from another in the same section.

So it is with leucocytic infiltration, which seems quite capricious in its appearance. The suggestion has been made (Goormaghtigh and Amerlinck) that both hyperplasia and leucocytic infiltration may be determined to some extent by the presence or absence of retained secretion. Such a suggestion is not supported by the material which I have had the opportunity of examining.

Hyperplasia and leucocytic infiltration may be pronounced in ducts which are not dilated and do not appear to contain any secretion, and may be totally absent from cysts filled with secretion. Moreover, hyperplasia may be unaccompanied by any striking degree of leucocytic invasion, and the latter may occur in the absence of any marked condition of hyperplasia.

The foregoing observations have been made almost entirely on male mice. Female mice have not been introduced very much into the discussion because there is not such a clear distinction to be seen in the mammæ of females between those treated with œstrogen and untreated controls. Observations, however, have been made on female mice, and no essential difference has been found between the results of the persistent administration of œstrin to male and female mice respectively.
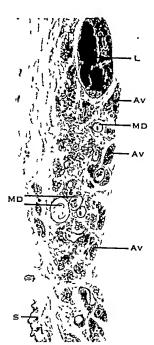
FIG 170.—Advanced degree of gynæcomastia and cystic mastopathy induced in male mouse by applications of equilin for a period of 246 days. S, Skin, L, Lymph-gland, MD, Dilated mammary ducts (cysts), Av, Alveolar formations (adenomata?). (× 12.)

6. Benign Adenoma.—As already mentioned, the distribution in the breast of the changes induced by œstrin may be irregular, some parts of a gland showing perhaps advanced changes while other parts appear almost unaffected. This irregularity may result in the development of local collections of proliferated ducts which might conceivably be regarded as adenomata. And when the treatment with œstrogen has been prolonged, groups of alveolar formations also sometimes appear here and there (*Figs.* 168–170). Whether these alveolar formations, which in some specimens are profusely scattered through the mamma (*Fig.* 170) after

prolonged œstrogenic treatment, can be properly termed adenomata or not it is difficult to decide. A substantial development of fibrous tissue does not commonly happen in mice, and I have not seen in these animals any bulky, well-defined, and almost completely encapsulated fibro-adenomata comparable with those innocent tumours which occur in women and also in rats and dogs. If, however, these local collections of proliferated ducts and alveolar formations in the mouse are to be described correctly as adenomata, it is worth remarking that they appear to react to œstrin in the same manner as the rest of the mammary tissue. Therefore it appears reasonable to suppose that, equally with other parts of the breast, they might ultimately become the seat of cancer, without necessarily being peculiarly liable to this change. (See ADDENDUM I.)

7. **Mammary Cancer.**—This has been an uncommon development among the mice in our own experiments. With the males there has been but 1 example among 116 individuals treated with various œstrogenic compounds. (See ADDENDUM II.)

The infrequency of mammary cancer in our mice after the regular and prolonged administration of œstrin is in contrast with Lacassagne's results which I have mentioned earlier. But Lacassagne found that in the males of one of the strains of mice which he used no mammary tumours were induced by œstrin. The paucity of malignant growths among our male mice might therefore be explained, perhaps, by a natural refractoriness. Mice belonging to a recognized and pure strain have not been available for our own experiments. We have used stock mice, all purchased from the same dealer, and spontaneous cancer of the mamma among the females of this stock appears to be an uncommon occurrence. There may be other than familial causes for the infrequency of cancer in our treated males, but the further consideration of this matter involves too much hypothesis and too little ascertained fact to be profitable. Whatever the explanation may be, it does appear established that in certain strains of mice, if not in all, the prolonged administration of œstrin leads to an increased liability of the animal so treated, whether male or female, to suffer from cancer of the breast.

To say that œstrin induces cancer of the mamma in mice would, I think, not be justifiable in the present state of our knowledge. Possibly the part played by œstrin in this connection is to put the mamma in such a condition that it is liable to become the seat of cancer, which is rather a different proposition from the assertion that œstrin induces carcinoma. The administration of œstrin to mice in sufficient amounts over a long enough period is, as our experiments have shown, frequently followed by cystic mastopathy. And reasons can be advanced for regarding this condition as a preparatory stage toward cancer—that is to say, as a precancerous state.

DISCUSSION

An association between cystic mastopathy and mammary cancer in women has been thought to exist by some clinicians and pathologists for more than half a century. Sir Henry Butlin used to teach thirty years ago that chronic mastitis, as the condition used to be called, with or without the presence of obvious cysts, is probably by far the most common predisposing condition in cancer of the breast; and in a generation earlier a similar opinion was held by Sir James Paget.

At the present day there are varying views as to the frequency with which mammary cancer is preceded by, or associated with, chronic cystic mastopathy.

Some (Cappell) will place their association as recognizable in nearly 100 per cent of all cases of cancer of the breast, while yet others (Campbell) believe that the incidence of cancer following chronic cystic mastopathy is no higher than in breasts which were previously normal. The difference of opinion between those who do and those who do not hold that cystic mastopathy is a precancerous state is perhaps, as Campbell has recently suggested, largely the result of the different bases for their conclusions, the former being guided by histological inquiry and the latter mainly by clinical experience.

As remarked already, the more serious feature of cystic mastopathy from the prognostic standpoint appears to be, not the presence of cysts, but the presence of epithelial hyperplasia. The only sure way of recognizing the presence of cystic mastopathy, when the dilatation of the mammary ducts is insufficient to cause the presence of cysts large enough to be appreciated by palpation or to be seen with the naked eye, is by the examination of microscopical sections. Therefore it would seen advisable to discard all opinions as to its frequency as a forerunner or accompaniment of mammary cancer which depend upon clinical impressions only.

Largely through the teaching of Sir Lenthal Cheatle and his colleagues it has become generally admitted now that the old term ' chronic cystic mastitis ' is a misnomer, the condition not being essentially of an inflammatory nature. For this reason the term ' cystic mastopathy ' has been used in this paper, although, possibly, a more explicit and better one might be ' œstrogenic mastopathy '.

In our experiments dilatation of the mammary ducts was never observed in male mice except in those which had been treated by a compound known to be œstrogenic. On the other hand, dilatation of mammary ducts was found in 59 per cent of male mice which had been treated with bi-weekly applications of œstrin over a period of fifty days or longer, and was usually accompanied by some degree of epithelial hyperplasia. In other words, cystic mastopathy was never seen in the males apart from treatment with œstrogens, whereas it was commonly present in those which had been treated with œstrin, and was often present following the administration of certain other compounds closely allied to œstrin.

The collective experience of those who have investigated the influence of the ovaries or of œstrin itself upon the mammæ of mice seems to show that cancer of the breast also is, in part at least, dependent upon this influence.

When the problem of human mammary cancer is considered in the light of the facts set out in this paper, it would seem that a temporary dilatation of the mammary ducts in a woman prior to the menopause might be regarded as a purely physiological condition. A persistent dilatation of the ducts, if such a condition were detected, would, however, give rise to some anxiety at whatever age it occurred. It would be presumptive evidence of an abnormal production of œstrogen, or an exaggerated responsiveness to its influence on the part of the mamma, or a diminution of the natural antagonism to œstrogenic action in that individual. If such a persistent dilatation were accompanied by hyperplasia of the epithelium, a more advanced stage of the over-reaction to œstrin would be recognized, and the anxiety as to the likelihood of cancer appearing in the future would be increased correspondingly.

Accepting œstrogens as the cause of cystic mastopathy, and this as a common precursor of cancer, how, it may be asked, could this knowledge be applied for the prevention or treatment of cancer of the breast in women ? To-day the reply

would be that it is well to understand the pathological causes and processes of any disease, and also to diagnose abnormal conditions in the mamma at the earliest stage possible, and particularly before the morbid state has progressed beyond recall.

There does not appear to be any insurmountable obstacle to the recognition in an individual of an abnormal production or retention of œstrogen; the amount present at different times in the blood and urine is capable of fairly accurate assay. On the other hand, once the necessity for such tests is appreciated, it can hardly be doubted that means will be found for ascertaining also what may be described as the susceptibility of any individual to the influence of œstrin. Thus the rate of disappearance of œstrin injected into the blood-stream already can be ascertained by experiment, and such an investigation might throw light on the cause of excessive reactivity to the influence of œstrin.

Natural antagonisms, both to the production of œstrin and to its action, exist in the body—antagonisms which can be recognized in the regulation of the œstrous cycle. For example, progestin, the hormone, or one of the hormones, derived from the corpus luteum, is in several respects an opponent in the living organism to the activities of œstrin. It seems not impossible that such natural agencies, when their characters are better understood, and the active substances themselves are more easily obtainable, might be utilized to adjust the balance, the aberration from which appears to be the cause of cystic mastopathy. Many of the effects of œstrin are reversible, and tissues which have undergone changes under its temporary influence return rapidly to their former state after the effective supply of œstrin has been withheld. This reversibility seems to reveal therapeutic possibilities, in spite of the fact that dilatation of the mammary ducts may persist for a considerable time after œstrin has been withheld. That mammary cysts do not speedily disappear after the supply of œstrin has been stopped does not, however, lessen the importance of an early diagnosis in women of the conditions which lead to cystic mastopathy, nor does it destroy every hope of providing a remedy. Success in such endeavours, it may be thought, would bring cystic mastopathy into the list of preventable diseases. And if, as many have supposed, cystic mastopathy is in fact a frequent precursor of cancer, it may be justifiable to hope that its early recognition and cure will render cancer of the breast to some, and perhaps to a large, extent an avoidable condition.

So far as concerns the cure of an established mammary cancer, experimental investigation of the action of the ovaries and of œstrin has brought to light no material for an increase of optimism. It has shown that ovariotomy, if performed early in life, may prevent cancer of the breast in mice; unfortunately it has also shown that little or no such preventive action follows an ovariotomy late in life, even though it be done prior to the appearance of any mammary tumour. That is to say, if the ovaries have exercised their function of producing œstrin over a sufficient length of time before their removal, cancer of the breast will not be prevented by ovariotomy. Nor will removal of the ovaries materially affect the course of a mammary cancer already present.

Many surgeons will remember the brief wave of optimism with which ovariotomy was regarded thirty years ago by a few enthusiasts as a treatment for inoperable carcinoma of the breast. Sir George Beatson, who introduced the procedure, was led to it by a recognition of the relationship between the mamma and the ovary. He did not regard the operation as a cure, but thought that,

combined with the administration of thyroid gland, it had a favourable influence on the local condition in the mamma itself. He stated clearly that visceral metastatic deposits were not influenced by the treatment. Some of his followers, however, were not so judicious, and for a short while there were surgeons who believed the operation to have some curative value.

Before concluding this paper reference may be made to the mammary changes which have occurred as sequels to the prolonged administration to male mice of œstrogens other than œstrin. It would be premature to discuss these results in detail because the work is not sufficiently advanced; they are summarized in *Table III*, and show, at least, that several of these compounds will induce pathological changes in the mamma of the mouse.

Table III.—EFFECTS ON THE MAMMÆ OF MALE MICE OF ADMINISTERING VARIOUS ŒSTROGENS, OTHER THAN ŒSTRIN, FOR PROLONGED PERIODS (FIFTY DAYS OR MORE)

ŒSTROGEN	SOURCE	SOLVENT AND CONCENTRATION	NUMBER OF MAMMÆ EXAMINED	NUMBER WITH GYNÆCOMASTIA	NUMBER WITH CYSTIC MASTOPATHY	CANCER
Ketomethoxyœstrin	Girard Cook	% Benzene 0·1	29	11	13	0
Dihydroxyœstrin (Dimenformon)	Organon Laboratories	Alcohol 0·1	5	0	0	0
Trihydroxyœstrin (Theelol)	Parke, Davis & Co.	Alcohol 0·1	4	3	3	0
Equilenin	Girard	Benzene 0·1	5	1	1	0
Equilin	Girard	Benzene 0·1	10	2	0	0
9 : 10–Dihydroxy–9 : 10–di–*n*–propyl–9 : 10–dihydro–1 : 2 : 5 : 6–dibenzanthracene ..	Lawson*	Benzene 0·3	15	8	5	0
9 : 10–Dihydroxy–9 : 10–di–*n*–butyl–9 : 10–dihydro–1 : 2 : 5 : 6–dibenzanthracene ..	Cook†	Benzene 0·3	9	0	0	0

*COOK, J. W., DODDS, E. C., HEWETT, C. L., and LAWSON, W., *Proc. Roy. Soc.*, 1934, cxiv, 272.
† COOK, J. W., *Jour. Chem. Soc.*, 1931, 489.

SUMMARY

1. The earliest pathological effect of œstrin observed in the mammæ of male mice is a proliferation of the mammary ducts, that is to say, *gynæcomastia*. This proliferation of ducts is occasionally accompanied, especially when the treatment has been prolonged, by the formation of what look like clusters of acini.

2. Speedily following the proliferation of ducts is their dilatation, with the formation of *mammary cysts*.

3. The next stage is that of hyperplasia of the epithelium lining the ducts, sometimes accompanied by an increase of the periductal stroma. This stage of hyperplasia combined with the presence of cysts, represents the 'chronic cystic mastitis' of the old, and the 'cystic mastopathy' of the new terminology. In view of its causation it might perhaps better be termed 'œstrogenic mastopathy'. In advanced cases epithelial anaplasia may be seen in the ducts.

All these foregoing changes are produced by œstrin, in the same sequence, in both male and female mice.

4. The proliferative and other effects of œstrin on the mamma are often distributed in different degrees throughout the gland, and a pronounced local proliferation perhaps may be in the mouse the equivalent of a benign adenoma in a woman.

5. In some of the mice treated with œstrin, whether male or female, carcinoma of the breast is apt to develop. Lacassagne states that this development in any individual mouse appears to depend in part at least upon that individual's responsiveness to œstrin. This responsiveness in mice, he states, may be an inherited character. It is a measurable quality and varies greatly among different pure-bred strains.

6. In women the output of œstrogens and the rapidity of their disappearance from the blood-stream can be estimated. Other factors which determine an individual's responsiveness to œstrogens can hardly be regarded as beyond the scope of future pathological inquiry.

7. Accepting these premises, it would appear possible to ascertain in some measure the liability of any individual woman to suffer from cystic mastopathy and from cancer of the breast before such conditions had actually developed. In other words it would be possible to anticipate the much desired early diagnosis of cancer of the breast by the recognition of a state in which cancer, though not yet present, is likely at some time or other to arise.

8. There is reason to expect that any divergence from a normal physiological equilibrium between the output of œstrogens and their antagonists may prove adjustable by artificial means.

9. If these conclusions are supported by experience, it will be possible to regard cancer of the breast to some extent as a preventable disease.

ADDENDA

ADDENDUM I.—Further study of the action of different œstrogens has shown that the mamma does not respond in the same way to every œstrogen used. Œstrin, for example, readily causes proliferation and dilatation of the ducts, but has little tendency to induce the development of alveoli. Equilin, on the other hand, has little if any tendency to cause proliferation and dilatation of the ducts, but apparently assists in the formation of alveoli. These differences in action between the various known œstrogenic compounds are at present being investigated.

ADDENDUM II.—Since this paper was written another male mouse of the series has developed mammary cancer. Of 125 male mice treated with repeated applications of œstrin and surviving for 100 days or more, 2 have now shown mammary cancer. Twenty-six of the total number of mice had been castrated prior to the administration of œstrin, and both instances of mammary cancer have occurred in this group of castrated mice.

I should like to mention with gratitude our debt to Dr. Girard, without whose generosity a large part of this inquiry could hardly have been carried out. He has presented us with considerable amounts of œstrin, equilin, and equilenin which had been prepared by himself in a pure crystalline state. We also have to thank the Organon Laboratories and Messrs. Parke, Davis and Company for supplying us with samples of dihydroxyœstrin and trihydroxyœstrin. It is a pleasure to mention these several kindnesses, and also to acknowledge the valued co-operation of my colleagues at this Institute, and my special indebtedness to Professor J. W. Cook. The microscopical sections and the photographic reproductions are the work of our technicians, Messrs. W. Davis and E. W. Woollard.

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THE INNERVATION AND MUSCULAR ACTIVITIES OF THE DISTAL COLON: WITH A NOTE ON THE SURGICAL TREATMENT OF CONSTIPATION*

By HUGH C. TRUMBLE

SURGEON TO OUT-PATIENTS, ALFRED HOSPITAL; SURGEON TO AUSTIN HOSPITAL, MELBOURNE

IN common with other parts of the alimentary canal, the distal colon is capable of peristaltic contractions. In this region, however, peristalsis seems to be kept in abeyance for long periods, so that waste material may accumulate and be stored until it becomes convenient to evacuate the fæcal mass. Holzknecht[1] pointed out that the progressive slowing of the rate of the onward passage of the contents of the gut, which is to be noted from the duodenum to the rectum, is not due to a corresponding weakening or slowing of the rate of peristalsis, but to an increase in the length of the intervals between movements. Thus, whilst in man peristaltic movements may be observed frequently in the jejunum, the colon is practically always at rest, only three or four powerful movements of brief duration occurring in twenty-four hours. In the rectum movements are still more infrequent. It is obvious that delays are of service to the animal, in that time is afforded for the completion of digestion and absorption in the small intestine and proximal colon, whilst the storage of fæces which takes place in the distal colon is a distinct convenience. This storage results in the accumulation of a large amount of material for the evacuation of which a special neuromuscular apparatus has been evolved. When this apparatus is brought into action, mass evacuation or defæcation results.

It is proposed to consider here some aspects of the specialized functions of storage of fæces and defæcation, to record certain physiological and clinical observations, and finally, to discuss briefly the surgical treatment of constipation. Peristalsis will not be considered in detail, but for the purpose of this paper it is of importance to note that in animals, at any rate, peristaltic waves continue to propel the contents of the gut after all of the extrinsic nerves have been severed and allowed to degenerate, and that such a state of affairs appears to be compatible with quite good function of the alimentary canal (Langley and Magnus[2]). Peristalsis appears to be a neuromuscular phenomenon involving a nervous reflex subserved by the intrinsic nerve plexuses of the gut. That peristalsis may be controlled by way of the extrinsic nerves will appear later.

THE EXTRINSIC NERVES OF THE DISTAL COLON

By 'distal' colon is meant that portion which normally contains formed fæces and is emptied during defæcation (Elliott and Barclay-Smith[3]). In carnivora this includes most of the colon, in man that portion between the region of the splenic flexure and the anus.

Nomenclature.—It is proposed to use the nomenclature adopted by Langley and Anderson.[4]

Anatomy.—The plan of the autonomic nervous outflows to the colon in cats, rabbits, and dogs was discussed in detail by Langley and Anderson in another paper.[5] A description of the outflows, as seen in various animals and man, is given by the author in a separate paper.[6] For the convenience of the reader, diagrams showing the plan on which the nerves concerned are laid down in the dog and in man are included here (*Figs.* 171, 172).

The distal colon receives nerve-fibres from the lumbar cord (upper set— Langley) and from the sacral cord (lower set). The segments giving origin to the
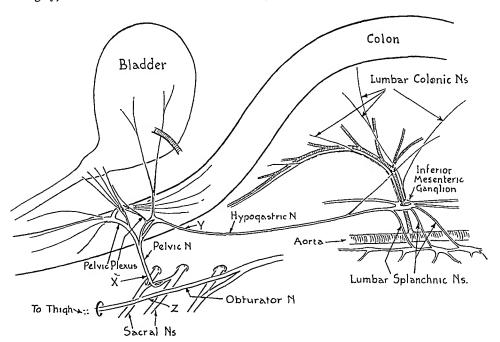
FIG. 171.—Diagrammatic representation of the nerves in the lumbar and sacral outflows of the autonomic nervous system in the dog. The inferior or lumbar splanchnic nerves pass from the lumbar trunks forwards and downwards to the region of the inferior mesenteric ganglia. A contribution from the cœliac ganglion also joins the ganglionic ring, which encircles the inferior mesenteric artery, and contains several small ganglia. From the ring arise numerous nerves which pass to the colon, and the two hypogastric nerves. which pass into the pelvis to enter the pelvic plexuses. From certain of the sacral nerves (mainly the second) twigs arise which join to form the pelvic nerves, one on each side of the body. The pelvic nerves pass into the pelvic plexuses. From these numerous nerves pass to the pelvic viscera.

lower-limb plexus intervene between the two sets. Langley showed that in animals the two groups of visceral nerves and the limb plexus arise commonly from certain definite segments of the spinal cord, but that variations are frequently to be observed. He described the usual arrangement as median, whilst pre-fixed and post-fixed plexuses were designated anterior and posterior respectively. Thus in rabbits with an anterior arrangement the main sympathetic effect on the colon was seen on stimulating the third and fourth lumbar nerves, whilst in the posterior type the effect was best on stimulating the fourth and fifth lumbar nerves.

As regards the physiological plan on which the nerves are laid down, it is

assumed that the reader is familiar with the general features of the autonomic nervous system as described by Gaskell and Langley. *Fig.* 173 will serve to illustrate some of the chief reflex arcs in the portion of the system under consideration. On the afferent side (receptor neurones of Gaskell) the fibres of both the lumbar and sacral outflows pass from the viscera by way of the posterior spinal roots to the spinal cord. From cells in the grey matter of the lumbar cord arise axones which pass by way of the ventral roots, lumbar nerves, white rami, sympathetic trunks, and inferior splanchnic nerves, to end by arborizing about cells in the inferior mesenteric ganglia situated further afield in the hypogastric nerves or pelvic plexuses. These fibres, which were designated by Gaskell as 'connector', by
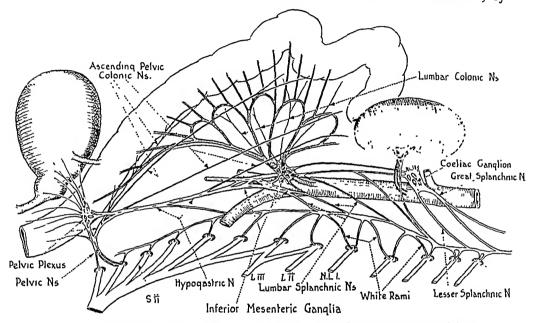
FIG. 172.—Diagrammatic representation of the nerves of the lumbar and sacral outflows of the auto-nomic nervous system in man. Note the striking resemblance in general plan to that in the dog as depicted in *Fig.* 171. The inferior mesenteric 'ganglion' is again not discrete but is rather a ganglionated network pierced by the inferior mesenteric artery. From the network numerous nerves pass to the colon and rectum. The pelvic nerves arise mainly from the third and fourth sacral nerves and join the hypo-gastric nerves to form the pelvic plexuses. The pelvic colonic nerves radiate as shown to reach that part of the colon supplied by the inferior mesenteric artery. Some of the uppermost nerves run for a time in company with the hypogastric nerves, as described recently by Telford and Stopford. The colon and the kidney are reflected ventrally.

Langley as 'pre-ganglionic', fibres, may divide and send branches to more than one ganglion cell, and some of these branches may cross the mid-line to reach ganglia of the opposite side of the body. From cells in the grey matter of the sacral segments of the spinal cord fibres arise which pass by way of the sacral ventral roots, sacral nerves, and pelvic nerves through the pelvic plexuses to end by arbor-izing about nerve-cells situated on, or in, the walls of the pelvic viscera. Thus the cell stations of this outflow are further removed from the central nervous system than in the case of the lumbar outflow. As a general rule the afferent fibres, con-stituting the receptor elements of the reflex arcs, and the connector or pre-ganglionic fibres are medullated, whilst the effector or post-ganglionic fibres are non-medullated. There are, however, exceptions to this rule.

It is reasonably certain that centres exist at higher levels in the central nervous system which exert a controlling influence on the arcs just described. These higher connections will not be considered in this paper.
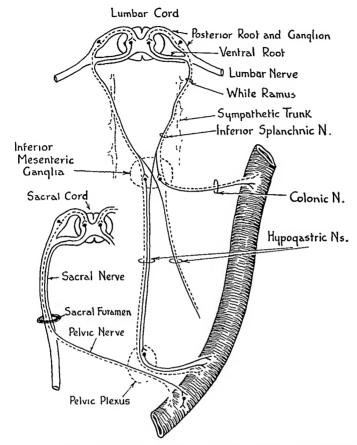
FIG. 173—Diagrammatic representation of some of the more important reflex arcs in the lumbar and sacral outflows of the autonomic nervous system Afferent or receptor fibres are represented by interrupted lines Their cell bodies are situated in the posterior root ganglia Pre-ganglionic or connector fibres have their cells in the lateral horns of the grey matter of the spinal cord, and their fibres pass out to link up with cells situated as shown. The cells of the post-ganglionic or effector neurones of the lumbar outflow are situated in the inferior mesenteric ganglia or ganglia of the pelvic plexuses, whilst those of the effector neurones of the sacral set are situated in the plexuses on or in the wall of the colon. (For further description *see* text)

PHYSIOLOGICAL ACTION OF THE EXTRINSIC NERVES OF THE DISTAL COLON

The Lumbar Nerves

In the course of many experiments on dogs the author has frequently stimulated the inferior splanchnic nerves and branches of the inferior mesenteric ganglion, without ever obtaining other than inhibitory effects upon the colon. The sphincter ani was not observed. Langley[1] noted occasional motor effects upon the colon on stimulation of the nerves of the lumbar outflow in rabbits and cats. Other

writers have described motor effects in dogs. On the other hand, section of the inferior splanchnic nerves has sometimes, but not always, been followed immediately by an astonishing increase of tone, the colon hardening and shortening quite forcibly, very occasionally showing also a series of peristaltic waves. It was pointed out by Bayliss and Starling[7] that there was difficulty in demonstrating any activity of the gut whilst its thoraco-lumbar nerve-supply was intact; and also that stimulation of any sensory nerve served to inhibit the gut, if the splanchnic nerves and spinal cord were unharmed. Surgeons practically never see true peristalsis in human beings when operating in the abdomen except in patients under high spinal anæsthesia.

Apparently the gut is reflexly inhibited when the abdomen is opened, and at least one limb of the arc runs in the splanchnic nerves (thoracic, in the case of the small gut; lumbar, in the case of the colon). Section of the inferior splanchnic nerves or the corresponding white rami, or of the distal branches of the inferior mesenteric ganglion, releases the colon from reflex inhibition. Spinal anæsthesia acts similarly. The author has frequently observed an immediate 'release' in dogs following upon section of the inferior splanchnic nerves. This 'release'
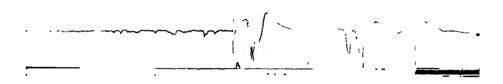
FIG. 174.—Enterographic record of the contractions of the circular muscle coat of the distal colon in a macaque monkey, showing the 'release phenomenon'. The animal was anæsthetized and immersed in a bath of warm Ringer's solution. For a period of about twenty minutes prior to the point marked A, the colon was inert and caused very little movement of the recording lever. At the point A the inferior mesenteric ganglionated network was crushed. Almost immediately the colon became very active, and a series of peristaltic waves starting near the hepatic flexure passed downwards. Contraction of the circular muscle at the site of attachment of the enterograph caused a downward movement of the recording lever. A decrease in tone followed each peristaltic wave. The time-marker records periods of five seconds.

is indicated by a rapid increase in tone of both coats and increased response to stimulation applied locally to the gut or through the medium of the pelvic nerve. The most dramatic immediate 'release' observed occurred, however, in a macaque monkey. In *Fig.* 174 is seen an enterographic record of contractions of the circular coat of the distal colon. The animal was anæsthetized (ether) and the abdomen opened, after which it was immersed in a bath of warm Ringer's solution. The colon was moderately distended throughout its length. An enterograph was attached transversely to the descending colon about 8 in. from the anus. For about twenty minutes the gut was exceedingly inert and the recording lever showed very little movement. The fibres of the nerve network in the region of the inferior mesenteric ganglion were then crushed. Almost immediately peristaltic waves originating near the hepatic flexure began to pass down the colon to the anus. Fæces were passed freely. The tracing shows well a series of powerful waves. It is worth noting that they are not preceded, but followed, by loss of tone of the circular coat.

Twice, in human beings, after section of the inferior splanchnic nerves for the relief of desperate constipation, the author has observed a similar but less dramatic release phenomenon. In each case the colon, which was distended and inert, became, after the nerve section, much more tonic, ringed in appearance, and readily responsive to pinching. As will be detailed later, certain forms of constipation appear to be permanently cured by the above procedure. In other words, the 'release' observed immediately after section of the inferior mesenteric nerves is not merely a passing phenomenon.

THE PELVIC NERVES

Elliott and Barclay-Smith,[3] after experimenting upon a wide range of animals, came to the conclusion that stimulation of the pelvic nerve caused contraction of both coats of the distal colon and rectum, the contraction of the longitudinal coat and recto-coccygeus following rapidly on stimulation and causing the gut to shorten and descend towards the pelvis, whilst the contraction of the circular coat was delayed, so that perhaps fifteen to twenty seconds after the commencement of stimulation a wave appeared at the upper end of the distal colon and then slowly passed down the gut to the anus.

Bayliss and Starling,[8] after experimenting on dogs and rabbits, stated that stimulation of the pelvic nerves (after destruction of the thoraco-lumbar outflow to the colon) caused rapid simultaneous contraction of both coats of the whole colon or any part thereof.

Langley and Anderson[5] experimented on cats, rabbits, and dogs. They found that stimulation of the pelvic nerves always caused contraction of the longitudinal coat and recto-coccygeus, whilst in the rabbit there was a delayed variable contraction of the circular coat, sometimes peristaltic in nature, sometimes spastic. In cats the circular effect was less marked, and in dogs there was only occasionally a belated peristaltic wave, which the observers thought might be accidental.

In view of the dissimilarity of the results obtained by the above observers, the author has carried out numerous investigations in dogs. Morphia has been administered as a routine procedure (1 to 1½ gr.) and followed by light ether anæsthesia. After opening the abdomen and exposing the nerves, the animals were usually placed in a bath of Ringer's solution, kept at about 37.5° C. The solution often became polluted by blood or dust from the animal's coat, even after preliminary washing, or by fæces passed during the experiment, so that, later, resort was had to the following technique. After making a long mid-line incision from sternum to pubis, the abdominal muscles were detached from the pelvic girdle by cutting their insertions close to the bone. This could be done practically bloodlessly. A piece of string was then passed through the lower end of each rectus muscle and served to retract these widely, and so to form a kind of parapet on each side of the abdomen, which banked up enough Ringer's solution to cover the gut. Access to the pelvis was greatly facilitated and trouble from contractions of the muscles of the belly wall almost eliminated. Warm Ringer's solution was poured freely into the trough so formed in the animal's abdomen throughout the experiment, and thus the liquid bathing the coils of gut was kept constantly fresh and clear.

Hooded electrodes were placed on the pelvic nerves, one or both as was convenient. In order to eliminate undesirable reflex effects, various procedures

were adopted at different times. Sometimes stimulation was applied with all nerves intact, sometimes after division of the inferior splanchnic nerves or hypogastric nerves. On many occasions the pelvic nerves were severed at their points of emergence from the sacral nerves. In a few cases the brain and spinal cord were entirely destroyed after tying the carotid and vertebral arteries in the neck. After this procedure artificial respiration was resorted to and anæsthesia discontinued. In all cases a weak faradic current easily appreciable by the tip of the tongue was used to stimulate the nerves. Sometimes the effect on the colon was observed but not recorded ; more often one or two enterographs were attached at different levels and a graphic record was obtained.

Certain effects were obtained quite constantly, irrespective of the state of preservation of the spinal cord, brain, or lumbar splanchnic nerves. One half of the bladder always went immediately into powerful spasm when the corresponding nerve was stimulated. Almost as rapidly and constantly the colon and rectum shortened and were drawn down towards the pelvis, there being no obvious
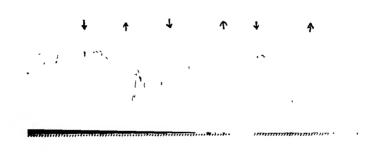
FIG. 175.—Enterographic record of the contractions of the circular muscle coat of a dog's colon, showing an 'Elliott' response. Under ether anæsthesia the carotid and vertebral arteries were tied and the brain was destroyed. Artificial respiration was commenced. The abdomen was opened, the central connections of the inferior mesenteric ganglion were divided, and an electrode was placed on the left pelvic nerve. The enterograph was attached just above the middle of the colon. The down-pointing arrows indicate the commencement, the up-pointing arrows the cessation, of faradic stimulation of the left pelvic nerve. Each stimulus was followed after an interval by a peristaltic wave commencing high up in the colon and passing down the gut. The time signal records periods of five seconds.

evidence of a unilateral effect. Up to this point the results were similar to those recorded by the above-mentioned observers. Upon the circular coat there was no constancy of effect. Often nothing more than a slight increase in amplitude of the pendulum beats, as shown on the tracing, was observed. In a few cases stimulation of one pelvic nerve was followed almost immediately by a spastic contraction of the circular coat, always best marked in the lower colon, but spreading sometimes well up towards the proximal third. This effect is similar to that described by Bayliss and Starling, but it was not often obtained. Much more frequently an 'Elliott response' was seen. The usual rapid shortening and descent of the colon was constantly observed, then after an interval of from ten to thirty seconds a wave appeared high up in the colon and slowly passed down the gut, frequently driving fæces before it. In *Fig.* 175 is seen a record of waves following stimulation of the left pelvic nerve in a dog after destruction of the brain and decentralization of the inferior mesenteric ganglion. The enterograph

was attached slightly above the mid-point of the colon so that the delay on the tracing between the stimulation and response does not represent the true latent period but includes also the time taken by the wave to pass from its point of origin down to the enterograph. In *Fig.* 176 the response is much more prompt. The enterograph was attached higher up on the colon than in the previous case, but
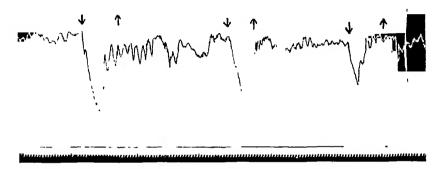
FIG. 176.—Enterographic record of the contractions of the circular muscle coat of a dog's colon, showing a more immediate response than in *Fig.* 175. The conditions of the experiment were the same as those detailed in the legend of *Fig.* 175, except that in this case the right pelvic nerve was stimulated and the enterograph was attached a little higher on the colon. Stimulation of the right pelvic nerve was followed almost immediately by the appearance of a peristaltic wave in the proximal third of the colon. This wave passed down the gut. Time = five seconds.

even so the effect is much more rapid than usual, and is very similar to that shown in *Fig.* 177, which is a record of the contractions of the longitudinal coat of the lower colon in the same dog obtained later in the experiment than *Fig.* 176. The
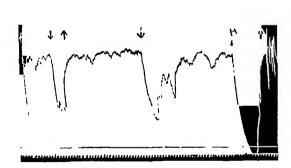
FIG. 177.—Enterographic record of the contractions of the longitudinal muscle coat of a dog's colon (distal segment). This record was obtained from the same animal as was that shown in *Fig.* 176, but later in the experiment. Stimulation of the right pelvic nerve was followed almost at once by a powerful contraction of the longitudinal coat and descent of the colon towards the pelvis. Arrows indicate commencement and cessation of faradic stimulation. The second stimulation evoked strong contraction of the longitudinal muscle coat which passed off although stimulation was continued. At the point marked H the current increased in strength. Another powerful contraction followed. Time = five seconds.

response is not of the 'Bayliss-Starling' type, because the contraction appeared high up and spread down the colon.

In some of the experiments, after a delay following stimulation a series of waves passing downwards from near the ileocolic junction has been observed.

Fig. 178 is a tracing recorded by two enterographs ; one (lower tracing) attached to the colon in its upper third, the other (upper tracing) in its middle third. Following stimulation there is a slight immediate effect on the upper tracing due to contraction of the longitudinal muscle, then after a considerable delay a powerful peristaltic wave at the upper enterograph (lower tracing), which reached the lower enterograph (upper tracing) after an interval. Then follow a series of waves passing from above down and affecting the lower enterograph (upper tracing) later than the upper. Sometimes the waves faded away before reaching the lower enterograph. *Fig.* 179 shows a second series of waves after the gut between the enterographs had been incised from the antimesenteric border so as to divide more than half of the tube. As will be seen, the waves had no difficulty in passing over the point of hemisection, although the contents of the gut exuded through the gaping wound. This observation is of interest in that it demonstrates that a distension of the gut in advance of a peristaltic wave is not necessary for the continuance of the latter.
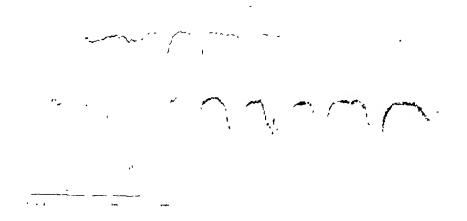
FIG. 178.—Enterographic records of contractions of the circular muscle coat of a dog's colon. Under general anæsthesia all four cerebral arteries were ligated in the neck and the brain was destroyed, after which artificial respiration was instituted. The abdomen was opened, the central connections of the inferior mesenteric ganglion were divided, and an electrode was placed on the right pelvic nerve. Two enterographs were attached to the colon, the upper on the gut recording below on the tracing. At the point L prolonged faradic stimulation of the right pelvic nerve was followed by a series of powerful waves passing downwards over the colon and recorded by both enterographs in turn. Some of the waves failed to reach the lower enterograph (upper tracing). Time = five seconds

On the whole the author's results are similar to those obtained by Elliott and Barclay-Smith. Langley did not immerse his animals in a saline bath, which may explain why he did not obtain a better response from the circular coat on stimulation of the pelvic nerves. The immediate contraction of the circular coat, noted by Bayliss and Starling, is sometimes, but not often, seen. Regarded from the standpoint of defæcation, the Elliott type of response would seem to be ideal. The author has not yet been able to discover why in one case one response is observed and in another a different effect. It remains to note that a true ' Elliott ' type of response has been obtained in dogs at different times after destruction of the brain and spinal cord, division of the pelvic nerves, hypogastric nerves, and the central connections of the inferior mesenteric ganglion. It would seem, therefore, that the impulse imparted to the pelvic nerve by experimental stimulation

is transmitted by fibres of the pelvic nerve direct to the neuromuscular mechanism of the colon and not by way of the spinal cord or hypogastric nerves.

The Effect on the Colon of Section of the Pelvic Nerves.—Elliott[9] noted that after section of both pelvic nerves in cats, fæcal retention did not ensue ; on the contrary, fæces were passed more frequently than usual. On the other hand, in rats after destruction of the lower part of the spinal cord, fæces accumulated in the colon, and he looked upon the gut as being paralysed.

Merzbacher[10] divided the sensory roots of the lumbar and sacral nerves in dogs, and observed that the animals no longer defæcated after the manner of dogs, co-ordinated movements of the tail, legs, and so on being absent. Fæces accumulated in the rectum without evoking strong contractions, and sometimes even protruded passively from the anus without exciting the sphincter to activity. Pellets of fæcal material would sometimes fall out whilst the animals were eating.
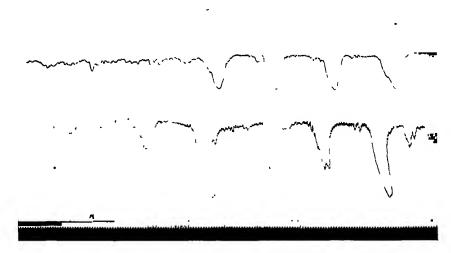
FIG. 179.—Records from the same animal as that from which *Fig.* 178 was obtained, but later in the experiment, after an incision had been made into the gut more than half dividing it, the wound being left gaping so that fæcal material forced down from above exuded through it, and did not pass into the segment of gut below the incision. Stimulation of the right pelvic nerve (point *iv*) was followed as before by the passage down the gut of a series of waves, which passed over the wounded area and were recorded by both enterographs. The upper tracing is from the segment of gut below the incision. Time = five seconds.

In the previous experiments, destruction of the spinal cord or roots of the lumbo-sacral nerves, or division of the pelvic nerves, involved much more than the pelvic nerve-supply to the colon. The author has endeavoured to eliminate such troubles as paralysis of skeletal muscles and the bladder by dividing the colonic branches of the pelvic plexus. This procedure, of course, results in the division of some fibres from the hypogastric nerves which run in company with the branches of the pelvic nerve to the colon and rectum.

Technique.—A small lower mid-line incision is made, and the abdomen is opened. The rectum is drawn upwards, and it is then possible to see several small branches from the pelvic plexus on each side ascending to enter the colonic wall and lying on its antero-lateral aspects just under the reflexion of the peritoneum. The latter is cut through with scissors, the visible nerves are divided,

together with small vessels accompanying them, and then a forefinger is introduced and the rectum is stripped away from the structures lying in front of and lateral to it, until the pelvic floor is reached. The stripping must be thorough.

This operation has been performed successfully in eleven dogs, and in all the after-history has been much as follows. After a few days, during which defæcation is usually much deranged, the animals begin to pass several small fæcal masses each day. Defæcation in normal dogs usually results in the extrusion of a fairly large amount of fæcal material, made up of an elongated mass often followed by one or more small oval nodules. This may be described as a mass evacuation, and occurs once, twice, or three times daily. In the experimental animals of this series, the comparatively infrequent mass evacuations were not seen, but, on the contrary, fæces were passed in the form of oval lumps, one at a time, frequently throughout the day and night. Only very occasionally was a mass passed at all comparable with that evacuated by normal dogs. During defæcation the animals squatted in the usual way, and behaved as though there
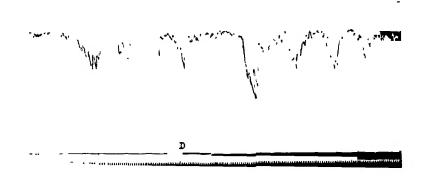
Fig. 180.—Enterographic record of the contractions of the circular muscle coat of a dog's colon. The colonic branches from the pelvic plexus were divided on Jan. 28, 1931. On Feb. 11 the animal was anæsthetized. The carotid and vertebral arteries were tied and the brain and spinal cord destroyed. Artificial respiration was instituted. The abdomen was opened and an enterograph attached to the colon in its proximal third, after which the animal was immersed in a bath of warm Ringer's solution. Spontaneous peristaltic waves passed at irregular intervals down the colon and fæcal material was passed. The tracing shows a series of waves following on a period of inactivity. At D the lumbar splanchnic nerves were stimulated, following which peristalsis was temporarily inhibited. Time = five seconds.

were nothing abnormal. The dogs were observed for periods of up to nine months' duration. One dog became ill (distemper) one month after operation, and died. The colon was contracted and completely empty as though it had been washed. A second dog became ill two weeks after operation. Under anæsthesia the brain and spinal cord were destroyed, and the abdomen was opened. Powerful spontaneous peristaltic waves were seen passing down the colon, and soft-formed fæces were passed into the bath. *Fig.* 180 is a tracing of the colonic movements in this animal, showing a series of spontaneous peristaltic waves. At the point D the inferior splanchnic nerves were stimulated, causing inhibition of peristalsis for a brief period.

Another dog was kept for nine months, apparently in perfect health except for the frequent passage of small fæcal masses. Under general anæsthesia the abdomen was opened, and the colon seen to be of smaller calibre than normal

and of good tone. After division of the central connections of the inferior mesenteric ganglion stimulation of the pelvic nerves had no effect on the colon, though the bladder contracted as usual. No peristalsis was seen until hypertonic saline was injected into the gut, after which powerful waves appeared. In one dog kept alive for two months, it was observed at the second operation that section of the inferior splanchnic nerves was followed by great increase in tone amounting to spasm of the colon. Another dog, in which the inferior splanchnic nerves were divided at the same time as the pelvic colonic nerves, defæcated as described above. At the second operation five weeks after the first the bowel was very tonic in appearance.

It may be noted here that in one dog which was not kept alive after the experiment, stimulation of either pelvic gave a good 'Elliott response'. The visible colonic nerves from the pelvic plexus on one side were then severed, after which stimulation of the corresponding pelvic nerve had no effect on the colon, although the bladder contracted normally. The same result was then obtained on the other side. Further, in none of the dogs which were observed after degenerative section of the pelvic colonic nerves did stimulation of the pelvic nerves evoke any response in the colon, although the bladder contracted normally. These observations make it fairly certain that the pelvic nerve-supply to the colon was destroyed, at least in great part. It is possible that minor branches to the sphincter ani region may have escaped destruction.

It was pointed out above, that division of the pelvic colonic nerves destroyed the colonic fibres from the sacral outflow, probably completely, but also resulted in the destruction of fibres from the lumbar outflow passing to the colon by way of the hypogastric nerves and the pelvic plexuses. The effect described above is not due to the destruction of the lumbar supply to the rectum or sphincter ani internus, as division of the hypogastric nerves or lumbar splanchnic nerves is not followed by loss of storage and mass evacuation. Further, in a few instances, both pelvic nerves have been divided proximal to the pelvic plexuses, whilst the hypogastric nerves remained unharmed. After this the animals defæcated in much the same fashion as did those in which the mixed pelvic colonic nerves had been destroyed.

It seems to be quite certain that the pelvic nerve carries fibres which when stimulated cause the distal colon to evacuate its contents. In normal defæcation some stimulus affects the afferent limb of an arc of which the above-mentioned fibres form the connector (Gaskell) or pre-ganglionic (Langley) segment. This action of the pelvic nerves has long been recognized. Further, it appears that the normal effect on the colon is similar to that described by Elliott as occurring in animals and frequently obtained by the author. It also seems likely that the pelvic nerves subserve a second important function, which does not appear to have been recognized. By virtue of this function the distal colon is able to store fæcal material for a considerable time. Thus dogs normally pass a large elongated stool, together with one or two smaller masses, about two or three times a day. Evidently material brought down to the distal colon by numerous peristaltic waves has been held up and welded into one typical mass or more. Much the same process must take place in human beings. After degenerative section of the pelvic colonic fibres or pelvic nerves, dogs do not store fæces, but pass numerous small oval masses throughout the day and night. Storage and mass evacuation

are abolished, and the inherent peristaltic mechanism of the alimentary canal, previously kept under control by the pelvic nerves, comes to the fore and material is passed as it becomes available. Fæcal retention is never seen. It is possible that excessive activity of those fibres of the pelvic nerve which subserve the 'storage' function might cause constipation, but the author has no evidence to support such a view. On the other hand, it would appear that diminished activity, or even destruction of the pelvic nerves, should not cause constipation *per se*. It is to be noted that lesions of the spinal cord or cauda equina involve the nerve-supply to skeletal muscle and the bladder, so that constipation might follow as an indirect result of widespread paralysis and infection.

It is possible that the fibres in the pelvic nerves which control and inhibit peristalsis in the distal colon may be to some extent under voluntary control. It is common experience that the act of defæcation may be deferred voluntarily, and the presence of some nervous mechanism subserving this action must be assumed. That the final pathway lies in the pelvic nerves rather than in the lumbar splanchnic nerves is suggested by observations in human beings with lesions of the cauda equina. All voluntary control is lost; and once defæcation is started it cannot be checked. Further, destruction of the lumbar splanchnic nerves is not followed by loss of control, if the pelvic nerves remain intact.

It is also quite likely that the pelvic nerves contain similar fibres destined to reach the bladder musculature and to exert on it a control similar to that just described in respect of the colonic musculature.

That one set of nerves should contain fibres subserving two functions which are to some extent antagonistic is by no means unique. Langley and Anderson[4] noted that whilst the usual effect upon the colon of stimulation of the lumbar splanchnic nerves was inhibitory in nature, motor effects were frequently to be observed. Barrington[11] noted that in cats section of the pelvic nerves was usually followed by loss of tone of the bladder musculature, but that on some occasions there followed instead a persistent contraction of the muscle. Barrington suggests the possibility of the presence in the pelvic nerves of fibres which inhibit the bladder, although he considers this unlikely.

A view which is widely held is that certain individuals are 'vagotonic', others 'sympatheticotonic' by nature. It is unnecessary to discuss what is meant by these terms. With regard to the colon, it is commonly stated that the two sets of nerves, sacral and lumbar, antagonize one another, and that under certain circumstances one or other may gain the upper hand and so upset the harmonious working of the viscus. Thus the lumbar outflow has been destroyed for the relief of constipation, in order to leave the sacral nerves unopposed. The author would put it that the procedure results in release of the intrinsic neuromuscular mechanism from abnormal reflex interference. When both pelvic and lumbar nerves are destroyed the intrinsic mechanism gains unfettered control, and succeeds in evacuating the contents of the distal colon.

Clinical Observations.—It occurred to the author that in cauda equina lesions in man defæcation should be similar to that just described. With a lesion below the second lumbar vertebra the pelvic nerve-fibres would be destroyed, whilst the lumbar sympathetic outflow would remain intact. The bladder would be involved as well as the colon. The effect of such a lesion should be seen best in a patient who was not debilitated or bedridden as a result of paralysis of skeletal

and bladder musculature, bed-sores, and infection of the urinary tract. It is obviously essential that no doubt should exist as to the completeness of the interruption of the nerves in question. Curiously enough, a suitable case came under the author's notice almost immediately.

A man of 32, a railway employee, was injured in a train accident on June 10, 1929. A skiagram taken after a short interval showed that the spine had been completely severed through the disc between the third and fourth lumbar vertebræ, the two bodies appearing side by side on the negative. There could be no reasonable doubt that the nerves of the cauda equina had been completely severed as well. After the injury retention of urine necessitated catheterization, and on July 13, suprapubic drainage was instituted. A period followed during which infection of the urinary tract and bedsores were troublesome.

The man was admitted to the Austin Hospital, and in February, 1930, there were no reflexes present at the knees or below. Weak voluntary extension was present at the knee on the right side, whilst on the left side it was somewhat stronger, and fair flexion was also present. Sensation was absent on the right side from just above the knee, and on the left side from just below the knee. Automatic voiding of urine was noted in June, 1930, the suprapubic wound having healed.

When first seen by the author in June, 1931, the patient was in excellent health, getting about in a wheeled chair. There was evidently a complete severance of all nerves below the second lumbar on the right side and the third lumbar on the left side. It was reasonably certain that the parasympathetic nerve-supply to the bladder and rectum was destroyed, whilst probably the lumbar sympathetic supply to the same organs was intact, or only partly destroyed. The man was in excellent health, able to get about in a wheeled chair, and to exercise his legs to some extent. The abdominal muscles were normal. There was no gross infection of the urinary tract.

A careful study of the functioning of the bladder and rectum was begun. When the bladder was distended the patient had a sensation of fullness in the hypogastrium. If he neglected to void urine it was passed involuntarily. In order to prevent this, he had got into the habit of attempting to micturate every two hours. By straining he was usually able to do so, often passing as much as 10 oz. of urine. There was no sensation evoked in the urethra by the passage of urine, but the feeling of distension was relieved.

From the point of view of this paper, defæcation was of more interest. Usually the patient took two alophen pills daily. Salts or cascara caused loss of control. During periods of constipation the patient complained of stomach-ache, referred to the centre of the abdomen. When the bowel was about to void there was some sort of sensation. The act could not then be delayed voluntarily. Enemata did not cause any definite sensation. A finger in the rectum was scarcely felt. The anal sphincters were atonic and patulous. Whilst on occasions a whole day would pass without the passage of any fæcal material, it was usually quite otherwise. As stated above, the patient habitually attempted to micturate every two hours, and frequently whilst doing so he passed fæces. Defæcation occurred commonly about three times daily, sometimes more, sometimes less. Almost invariably two, three, or four small soft, discrete, oval lumps were passed at each attempt, never a large mass approximating to the normal stool.

To all intents and purposes defæcation in this case was similar to that recorded above as occurring in animals after section of the pelvic colonic nerves. Mass defæcation was lost, storage was lost, and small fæcal masses were passed at frequent intervals, apparently as a result of peristaltic action.

THE EFFECT UPON THE COLON OF EXCISION OF THE RECTUM

Radical excision of the rectum is almost certain to result in the destruction of the pelvic nerve-supply to that part of the distal colon which is left behind after operation (see Fig. 172). As a rule after this procedure patients defæcate through a sigmoid colostomy. Constipation does not follow, as might be expected by the

proponents of the theory of unbalanced nerve action. On the contrary, fæces are usually passed involuntarily several times daily, and at each action it appears that several small amounts are extruded seriatim, as though by separate peristaltic waves. This effect is probably due to the removal of the influence of those fibres of the pelvic nerves which subserve storage of fæces. Although many of the fibres of the lumbar outflow to the colon are still intact, peristalsis cannot be inhibited voluntarily.

Practical Applications.—Royle,[12] in a paper published in 1924, stated that certain of his patients were relieved of constipation as a result of ramisection performed primarily for the relief of spastic paralysis of the lower limbs. Wade[13] subsequently practised an operation in which he divided on the left side the white rami from the first and the second lumbar nerves, the visceral branches of the lumbar sympathetic chain, and the trunk itself at the pelvic brim, in the treatment of cases of Hirschsprung's disease, with encouraging results. Judd and Adson[14] removed the greater part of the lumbar trunks on the left or on both sides with good results. The author has discussed these operations and described that designed and practised by himself in another paper.[15]

Rankin and Learmonth[16] designed an operation very similar to that of the author, but somewhat more extensive in its scope. In the author's operation the majority of the inferior splanchnic nerves and the cœliac root of the inferior mesenteric ganglion are divided near the origin of the inferior mesenteric artery from the aorta. Rankin and Learmonth divide the 'presacral' nerve and, tracing this upwards, remove the whole of the network of nerves in the region of the base of the inferior mesenteric artery. In effect, he removes what the author has called the 'inferior mesenteric ganglionated network' (see Fig. 172).

In all these operations the lumbar sympathetic outflow to the lower abdominal viscera is destroyed in greater or less part. As a result of further experience, the author believes that in most cases simple resection of part of the hypogastric nerves (or the 'presacral nerve') is sufficient to obtain the desired effect. On occasions it is desirable to destroy the sympathetic supply to the lower limbs as well as that to the viscera, and this is done by a bilateral lumbar sympathectomy, performed through a paramedian abdominal incision.

Selection of Cases and Type of Operation.—Three main groups may be described :—

1. The first group comprises cases in which there is severe constipation associated with gross dilatation of the colon, and includes cases of Hirschsprung's disease. The operation should be radical, aiming at destruction of the greater part of the lumbar sympathetic supply to the colon. This is best attained by Learmonth's or the author's operation. The approach is through the abdomen and the attack is directed at the inferior mesenteric ganglionated network. The operation may be tedious in the presence of much adipose and lymph-glandular tissue. The results are usually good, but in some cases not permanent.

2. The second group comprises cases in which there is severe constipation associated with chilblains or 'chilblain circulation' of the extremities. Many of these patients are very miserable as a result of the state of their bowels and the extreme irritation of chilblains. Operation in such cases is designed to relieve both conditions. Both lumbar trunks below the first lumbar ganglion are excised, usually at one sitting, through a paramedian abdominal incision. The results are most gratifying, both as regards bowel function and the circulation of the lower limbs.

3. In the third group are placed those cases in which extreme constipation, which is unresponsive to conservative measures, is associated with other troubles such as dysmenorrhœa, neurasthenia, indigestion, and poor health generally. The colon is usually not dilated and may appear to be quite tonic. When other measures have failed, resection of portion of the hypogastric nerves may be tried. This is a fairly simple operation. Usually the bowel function is much improved and this reacts favourably on the patient, particularly upon his mental state. The gut appears to be released from some baneful reflex interference. Dysmenorrhœa, if present, is relieved.

It is hardly necessary to state that no patient should be subjected to operation until conservative measures have been thoroughly tried out and have failed. On the other hand, intractable constipation may make a person very miserable, and an operation holding out some hope of relief should not be denied him when all other measures fail to give relief.

SUMMARY AND CONCLUSIONS

In considering the normal functions of the distal colon it is pointed out that the muscle coats of this portion of the gut are capable of powerful peristaltic contractions. Peristalsis continues in the gut quite satisfactorily after all of the extrinsic nerves are divided and allowed to degenerate. In the distal colon peristaltic action is apparently controlled and kept in abeyance for long periods by a superimposed influence which is exerted through the medium of the pelvic nerves. Thus storage of fæces is rendered possible until such time as it is convenient to evacuate the bowel. Activity of the muscular coats of the distal colon may be inhibited also by artificial stimulation of the nerves of the lumbar outflow, and probably this inhibitory influence operates as a result of reflex stimulation in the intact animal. Further, it is probable that abnormal reflex activity may be at the root of certain forms of constipation. Division of the nerves in question should, and often does, remove the inhibitory influence and relieve constipation. This release phenomenon is the basis of certain operations which are described in brief.

Mass evacuation or defæcation proper is rendered necessary and possible because of the capacity of the colon for storing fæces until it becomes convenient to defæcate. Storage is apparently a function controlled by the pelvic nerves, and when these are divided, the peristaltic action of the gut is released from the controlling influence and small amounts of fæcal material are passed at frequent intervals. Defæcation proper depends on the integrity of the pelvic nerves and is lost when these are destroyed. The effect on the distal colon of stimulation of the pelvic nerves in dogs is described. Usually the result is similar to that described by Elliott and Barclay-Smith. The muscle of the longitudinal coat contracts almost at once, shortening the colon and drawing it down towards the pelvis. After an interval a contraction of the circular coat begins at the upper end of the distal colon and spreads downwards, driving fæces before it. Sometimes this is followed by other waves of like nature.

Certain clinical observations are recorded which seem to lend support to the conclusions drawn from experiments in animals. After complete severance of the nerves of the cauda equina, a man passed small amounts of fæcal matter at intervals throughout the day, apparently having lost the power to store fæces,

and the faculty of mass defæcation. After excision of the rectum, which results in the destruction of most of the colonic branches of the pelvic plexus, the remaining *portion of the distal colon is deprived of* its pelvic nerve-supply and that part of the lumbar sympathetic nerve-supply which passes through the pelvic plexus. Fæces are usually passed through a sigmoid colostomy several times daily, and at each voiding several small amounts are passed at short intervals, evidently by peristaltic action. It would appear that the capacity for storage is lost and that the inherent peristaltic mechanism of the bowel, released from the controlling influence of the pelvic nerves, takes charge and expels fæces as they become available.

A brief description of certain operations which have been advocated in the treatment of desperate constipation is given. In all of these the lumbar outflow of the sympathetic nervous system to the lower abdominal viscera is destroyed to a greater or less extent. The beneficial effect is probably due to the release of the colonic musculature from abnormal reflex influences of an inhibitory nature such as may be observed experimentally when a sensory nerve is stimulated, the spinal cord and sympathetic nerves being intact. That it is not due to the ' unopposed ' action of the pelvic nerves is suggested by the fact that when the latter are destroyed, either in animals or man, constipation does not necessarily result, althought the lumbar sympathetic nerves remain intact.

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SHORT NOTES OF RARE OR OBSCURE CASES

POST-TYPHOID CHONDRITIS WITH ABSCESS FORMATION

By R. C. BROCK

SURGICAL TUTOR AND REGISTRAR, GUY'S HOSPITAL

POST-TYPHOID infection of costal cartilage must be a rare condition since reference to the standard text-books of medicine, surgery, and pathology reveals that little or nothing is said about it. Those authors that do mention it amongst the many possible complications and sequelæ of typhoid fever merely state that it may occur. Post-typhoid infection of bone appears to be less rare and is more fully described. The following case merits recording not only as an instance of post-typhoid chondritis, but also because it demonstrates the morbid anatomy of infection of costal cartilage by *B. paratyphosus B.*

HISTORY.—J. S., aged 32, a medical practitioner, developed a painful swelling in the neighbourhood of the inner end of the clavicle in May, 1934. The condition was associated with pyrexia and there was considerable pain in the adjacent muscles and those of the shoulder. He was compelled to rest in bed, and after two weeks the pain stopped and the acute swelling subsided. Towards the end of August pain was again noticed and a small lump appeared just below the inner end of the left clavicle and slowly increased in size.

ON EXAMINATION.—Examination revealed a smooth, almost painless, firm swelling situated very accurately over the first costal cartilage, to which it was attached. It could be ascertained with fair certainty that it did not arise in connection with sternum, rib, or clavicle. There were no other abnormal physical signs. X-ray examination of the bones of the neighbourhood and of the lungs was negative. In view of the apparent strict localization of the condition to the costal cartilage none of the suggested diagnoses of gumma, growth, or tubercle seemed likely. The acute onset with fever and pain was against them all. Tubercle, which was the most likely on the grounds of frequency, gives a soft fluctuating abscess and not a firm lump. The Wassermann reaction was negative. There remained the possibility of a post-typhoid infection as one of the few causes of the rare condition of costal chondritis.

Inquiry revealed the fact that in 1920 (fourteen years before) there had been an illness, suspected at the time to be paratyphoid fever, but unconfirmed as blood culture and the Widal reaction had both been negative. The Widal reaction was repeated and found to be positive to *B. paratyphosus B* in a dilution of 1–500. Muir and Ritchie, in their text-book of bacteriology, state that agglutination with a dilution of 1–25 is positive for *B. paratyphosus B.* The titre given was, therefore, very high. Examination of the stools and urine revealed no evidence that the patient was a carrier.

OPERATION.—Operation was performed in October, 1934, six months after the onset of symptoms. A slightly oblique incision was made over the first costal cartilage. The underlying pectoral muscle was found to be fibrous and indurated, and lying on the anterior surface of the first costal cartilage was a small abscess cavity with dense fibrous walls containing about 1 c.c. of thin yellow pus. On exposing the anterior surface of the cartilage more fully it was seen to be perforated in several places by small holes much as one sees in old worm-eaten furniture. (This appearance has been noticed before by the writer in the case of typhoid chondritis.) A probe could be passed into a definite abscess cavity in the interior of the cartilage, revealing that the condition was similar to a ' collar-stud ' abscess. Having regard to the anatomy of the part and the dense fibrosis around, there was a great temptation to be content with a liberal curettage of the affected area. As such a course would almost inevitably lead to persistent sinus formation, the whole costal cartilage was excised from sternum to rib attachment. This is the only certain way to prevent a chronic sinus following infection of a costal cartilage. The cavity left was plugged with a small flap of the overlying pectoral muscle and the wound was closed without drainage. Apart from a slight serous discharge from one portion of the wound for some twenty-four hours, healing occurred by primary union. *Fig. 181* shows the excised specimen. The irregular central abscess cavity and the ' worm-eaten ' appearance given by the cloacæ in the cartilage which led to the more superficial abscess are well seen.

FIG. 181.—Costal cartilage excised at operation.

Culture of the pus from the cavity gave a pure growth of *B. paratyphosus B.*

Muir and Ritchie state that the tendency to form abscesses from which the specific organism can be recovered is now recognized as a feature in the complications or sequelæ of infection with the *B. paratyphosus B.* In fact the organism was first isolated from such suppurative lesions.

SUBSEQUENT HISTORY.—During recent years the patient has been subject to attacks of lumbago and fibrositis. It will be interesting to see if these attacks disappear now that a definite focus of infection has been removed.

Commentary.—Points of interest in the case are :—

1. The diagnosis of a subacute inflammatory swelling over a costal cartilage as a post-typhoid abscess.

2. The complete excision of the infected area followed by rapid healing. The books state that a chronic sinus usually follows typhoid infection of bone or cartilage.

3. The morbid anatomy of the specimen removed.

4. The recovery of the organism in pure culture after a lapse of fourteen years.

AN ANOMALOUS DUODENAL POUCH

By J. C. BOILEAU GRANT

DEPARTMENT OF ANATOMY, UNIVERSITY OF TORONTO

THE anomalous bag or pouch of duodenal mucosa here depicted (*Figs.* 182, 183) was found in a male aged 47 years and was brought to my attention by a student (W. D.). It was about the size of the terminal phalanx of a finger, 25 mm. by 12 mm. It hung within the lumen of the gut like a hollow polypus whose mouth was directed towards the pylorus. It was attached by one lip of its slit-like mouth; the other lip was free, and on the margin of this free lip the common orifice of the bile and pancreatic ducts opened.

It is well known that the valvulæ conniventes in the region of the papilla of Vater have a characteristic arrangement; one forms a hood over the papilla, another descends from the papilla as a longitudinal fold, the plica longitudinalis duodeni. These could not be identified in this specimen. The interior of the pouch was smooth except for the presence of a longitudinal fold on its posterior wall.

FIG. 182.—A photograph of the pouch.
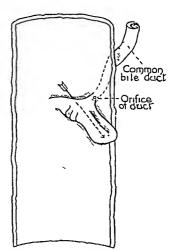
FIG. 183.—A sketch of the pouch.

Histological sections of the posterior wall of this pouch show that it consists of a reduplication of the entire mucous membrane of the gut—that is to say, the inner and outer surfaces are lined with villi which are supported by the usual reticular stroma, and in the middle, two layers of tunica muscularis mucosæ are applied to each other. No glands of Brunner are to be seen. That the tunica muscularis mucosæ is reduplicated is significant. Sections taken for comparison from adjacent parts of the duodenal wall make it clear that this point is not in question.

As to the cause of its formation, a variety of reasons will no doubt suggest themselves as possible. The actual cause, however, can only be surmised. It is more than probable that peristaltic action of the bowel had caused the pouch to increase in size. Had radiograms of an opaque meal been taken, the pocket would no doubt have filled and would have simulated a duodenal diverticulum. The site and outline of the pouch and the age of the patient would have tended to substantiate this suspicion.

That such a mass within the lumen of the gut might give rise to symptoms of ileus is evident. In fact, in the hospital record it is stated that the subject had had pain in the gall-bladder region for three years, that he was rarely free from pain for half a day at a time, and that he suffered from nausea and occasionally from vomiting after eating. The cause of death was septic bronchopneumonia.

A HUGE FIBRO-ADENOMA OF THE BREAST

By KENNETH MACKENZIE, AUCKLAND, N.Z.

A WOMAN, aged 34, said that for two years a tumour had been steadily growing in her left breast. She had gone for treatment to a religious revivalist and faith-healer and had been in his hands for many months. Three weeks ago ulceration had occurred and there had been a foul black discharge, the stench from which had driven her to seek medical advice. There had been no pain, but great incon-

FIG. 184 —Large fibro-adenoma of breast.

venience from the bulk and weight of the breast. Rapid deterioration in general health had taken place since the breaking-down had occurred.

Fig. 184 shows the condition that was present. There was no fixation of the mass to the chest wall, and removal was easy. Convalescence was uneventful, and two years later the woman was in excellent health.

The tumour weighed 35 *lb.* and was a fibro-adenoma.

SPONTANEOUS RUPTURE OF THE SPLEEN

By W. D. GALLOWAY,

ASSISTANT SURGEON, HUDDERSFIELD ROYAL INFIRMARY

MRS. F. H., aged 29, whilst kneading bread at 10.45 a.m. on March 17, 1934, was suddenly seized with severe pain in the left hypochondriac region. The pain, which came in spasms, grew rapidly worse and was felt in the left shoulder. The patient stated that she had fainted. She had had no illnesses of any note, had not suffered from malaria, and no history of injury however slight could be elicited after the most exhaustive interrogation. The last menstrual period occurred on March 10, 1934. Her periods up to the time of her last pregnancy had been regular, 3/28 with a normal loss ; since the birth of her last child, however, the menstrual ratio had been 7–8/28 and the loss excessive. The patient had two children, aged 3 years and 1 year respectively ; both were born by natural forces, and the subsequent puerperia as far as could be ascertained were normal. No miscarriages, no intermenstrual discharge. The bowels were regular, micturition was normal, and the patient had not vomited.

ON ADMISSION.— The temperature was 99° and the pulse 112. The patient's lips were cyanosed and the mucous membranes pale. There was no restlessness or air-hunger. She complained continually of pain in the left shoulder, and it was observed that when she was rolled on to the right side in an attempt to elicit movable dullness pain was urgently complained of in the right shoulder, but when she was allowed to sink back again into the recumbent

FIG 185 —Ruptured spleen

position the pain shifted with the altered position into the left shoulder again. This phenomenon of shifting pain in the shoulder was a marked feature of the case and was noticed and remarked on by all present. The abdomen moved well with respiration, was tumid and very tender, especially over the left hypochondrium ; there was no rigidity.

Per vaginam—the uterus was firm, bulky, and freely movable ; the fornices revealed no abnormality other than a marked tenderness in the pouch of Douglas.

DIAGNOSIS.—This was not made with certainty ; perforation of a hollow viscus and rupture of an isthmial pregnancy were considered.

OPERATION.—The abdomen was opened by a left paramedian incision about 5 in. long, about four-fifths being situated above the level of the umbilicus. When the peritoneum was incised only omentum was visible, but on manipulating this about a pint of blood gushed into the wound. The pelvis was at once explored, and both uterus, tubes, and ovaries were found to be normal.

A hand passed into the left hypochondrium detected clots, and this in turn led to a careful examination of the spleen, which seemed unduly friable and appeared to have a small irregular laceration on its diaphragmatic surface (*Fig.* 185). The incision was slightly lengthened and the spleen removed. Most of the blood and clots were evacuated and the peritoneal cavity was left comparatively dry. A transfusion of one pint of blood was administered at the end of the operation.

Fig. 186 shows a microscopical section of the spleen.
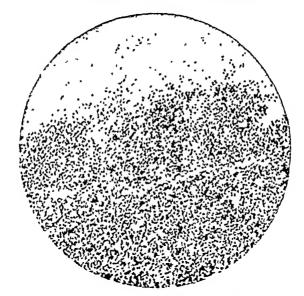
FIG. 186.—Microscopical section of spleen.

SUBSEQUENT PROGRESS.—A small abscess in the abdominal wound was opened on the tenth day, after which the incision healed uneventfully. On April 9 the patient developed an attack of thrombosis in the left leg which lasted four weeks. She was discharged on May 24 at her own request. She was seen on Dec. 13 and still appeared rather anæmic. The abdominal wound had healed well and no sign of an incisional hernia could be detected. She still complained of some œdema in the left leg towards the end of the day.

Observations.—

1. The complete absence of nausea and vomiting was noteworthy.

2. Shoulder pain, especially *pain moving from the uppermost shoulder to* the shoulder on which the patient was recumbent when turned from the supine to a lateral position, was a marked feature of the case.

3. A perusal of the literature seems to show that these cases are seldom correctly diagnosed before abdominal section ; but had the possibility of a spontaneous rupture of the spleen been entertained, this, together with the initial site of the pain and a consideration of the physical signs, should have suggested the correct diagnosis.

BIBLIOGRAPHY

SUSMAN, M. P., *Brit. Jour. Surg.*, 1927–8, xv, 47.
BAILEY, HAMILTON, *Ibid.*, 1930, xvii, 67.

SUPERNUMERARY CARPAL BONE

BY N. G. W. DAVIDSON, O.B.E.

VISITING SURGEON AND HONORARY LECTURER IN CLINICAL SURGERY, VICTORIA INFIRMARY, GLASGOW

IT is well recognized that supernumerary carpal bones do occur, and according to Kohler the most common is the os trapezoid secundarium. One, however, that
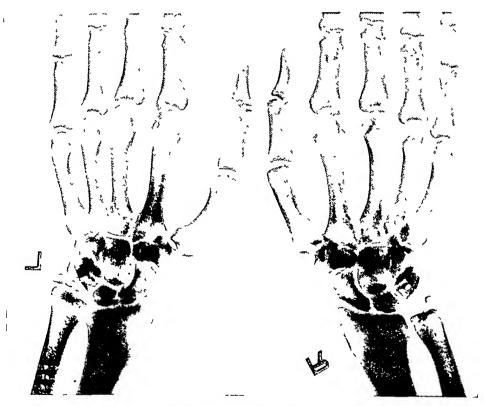
FIG. 187.—Supernumerary carpal bone

is rarely met with is the os triangulare or the os intermedium antibrachii. It has been described as being a unilateral condition, and I have been unable to find an example of it occurring bilaterally. There is some doubt as to the origin of the

bone. In some cases where the styloid process of the ulna has been detached and become enlarged and ceases to look like a fragment it has been considered as the origin. Non-traumatic cases have occurred, or at least been described, but the most reasonable explanation for the formation of this bone seems to be that given by Pfitzner—that it is due to a broken-off pseudo-arthrotically healed process of the styloid.

The present case, P. R., aged 22, gave a history of an accident in January, 1935, the accident being a twist to his left wrist. He informed us that for more than twelve months he had been finding discomfort in his wrist in making certain movements, and when making them he felt a click. On further questioning he informed us that he had 'broken' his wrist at the age of 16, and that the wrist had not felt right since then. Clinical examination revealed nothing that could be described as abnormal: no click could be elicited nor could the patient himself make the click voluntarily. An X-ray was taken, and a beautiful example of an os triangulare was seen (*Fig.* 187). It will be noted in the X-ray that the styloid process of the ulna has been broken off and that the typical triangular-shaped supernumerary carpal bone is well shown.

REVIEWS AND NOTICES OF BOOKS

St. Bartholomew's Hospital Reports. Edited by LORD HORDER OF ASHFORD, W. GIRLING BALL, RONALD G. CANTI, CHARLES F. HARRIS, WILFRED SHAW, H. H. WOOLLARD, R. C ELMSLIE, GEOFFREY EVANS, and J. PATERSON ROSS. Demy 8vo. Pp. 279 + xxiv. Illustrated. 1934. London: John Murray. 21s. net.

FOR the writer the 1934 volume of these reports has a note of personal sadness, for it contains a short obituary notice of William Foster Cross, whose colleague the reviewer was privileged to be at the Fishmongers Hall Hospital for Officers during the war. The biographer very happily summarizes Cross's chief characteristic as an anæsthetist when he says "that to be really appreciated as a man he had to be seen contending with a fractious surgeon and a difficult patient". Besides being a most competent anæsthetist, Cross was always obliging to those with whom he had to work, and his consideration and patience for nerve-shattered officers was extraordinary considering the claims he had on his time.

The problem of peptic ulcer is considered anatomically, pathologically, and surgically, in some very full and careful papers : we cannot find that the matter is advanced appreciably.

Professor Fraser, Sir Thomas Dunhill, and Dr. Spence similarly deal very thoroughly with the toxic goitre in its anatomical, physiological, and surgical aspects : this is a most comprehensive piece of work which brings the matter right up to date, and must be a most valuable guide to those who are interested in the treatment of patients suffering from this disease.

The Anatomy of Surgical Approaches. By L. C. KELLOGG, A.B., M.D., Professor of Anatomy, College of Medical Evangelists, Loma Linda and Los Angeles, California. Crown 8vo. Pp. 134 + x, with 29 illustrations. 1934. London. Baillière, Tindall & Cox. 7s. net.

THIS small volume appears to have been started with the idea of giving the surgeon an anatomical guide to certain operative procedures, but as the volume developed many details of surgical technique crept into the book and its original purpose has, therefore, been somewhat obscured. In our judgement, if it had been limited to the anatomy of surgical approaches it might have served a useful purpose, but it is scarcely possible to write even a superficial account of operative surgery within the scope of such a volume. It limits itself largely to the extremities and head and neck, dealing only with the nerves, arteries, and bones. The text is accurate, but a considerable amount of unnecessary elementary detail might be eliminated. The few line diagrams are helpful in making clearer what is described in the letterpress.

Surgical Applied Anatomy. By Sir FREDERICK TREVES, Bart., revised by C. C. CHOYCE, C.M.G., C.B.E., B.Sc., M.D., F.R.C.S., Professor of Surgery, University of London, etc. Ninth edition. F'cap. 8vo. Pp. 720, with 174 illustrations, including 66 in colour. 1934. London : Cassell & Co. Ltd. 14s. net.

To dip into a fresh edition of Treves' *Surgical Applied Anatomy* produces a feeling akin to the sorrow and regrets which are occasioned by visiting one's birthplace or preparatory school. Any new edition cannot be the same as our old friend, and therefore it is not so good. And where is the story which first aroused our interest in the viscus concerned ? Gone ! One feels one has lost an old friend, yet the vast store of anatomical detail remains : one can scarcely raise an anatomical question to which the answer cannot be found here. The new edition is well illustrated, is commendably accurate, and is nicely published. As the viewpoint of the surgeon has since Treves' day veered from the limbs to the abdomen, and more recently to the brain and thorax, so the space allotted to these different parts has gradually been amended ; but in the present edition the autonomic nervous system is not described in accordance with present-day beliefs.

There is a puzzling mixture of nomenclature which in a future edition it is hoped will be eliminated by the substitution of the Anatomical Society's nomenclature for the two now in use.

Illustrations of Regional Anatomy. By E. B. JAMIESON, M.D., Senior Demonstrator and Lecturer, Anatomy Department, University, Edinburgh. F'cap. 4to. Published in five sections : Section I, Central Nervous System, 48 plates, 7s. 6d. Section II, Head and Neck, 61 plates, 10s.   Section III, Abdomen, 37 plates, 5s. 6d.   Section IV, Pelvis, 30 plates, 3s. 6d.   Section V, Thorax, 27 plates, 4s.   1934.   Edinburgh : E. & S. Livingstone.   Complete set, 30s. net.

PROFESSOR JAMIESON's atlas of coloured diagrams of human anatomy is a delightful production. It is said they are 'paraphrases' of the author's blackboard diagrams, which must indeed be things of beauty. The plates are fitted on to looseleaf pillars and, printed on only one side of the page, may be pasted in notebooks. The body is divided into regions and is dealt with in five sections which do not include the arm or leg : this is, in our judgement, to be regretted, but no doubt cost was the deciding factor. At 30s. it seems a marvellously cheap production. As a member of the Sub-committee of the Anatomical Society which, after much labour, produced the nomenclature, the author rightly makes use of it, adding the B.N.A. terms in brackets when the names are medically different.

Handbook of Anæsthetics. By J. STUART ROSS, M.B., Ch.B., F.R.C.S.E., late Lecturer in Practical Anæsthetics, University of Edinburgh ; and H. P. FAIRLIE, M.D., Anæsthetist to the Western Infirmary, the Royal Hospital for Sick Children, and the Dental Hospital, Glasgow. Fourth edition. Crown 8vo. Pp. 299 + x, with 66 illustrations. 1935. Edinburgh : E. & S. Livingstone. 10s. 6d. net.

IN preparing the fourth edition of this popular little work on anæsthesia, Dr. Fairlie has shown excellent judgement in selecting what to discard and what to retain, and has brought his subject up to date, although cyclopropane and vinesthene have not been included, owing, probably, to these drugs being so recently introduced that the author found it difficult to express a practical view as to their properties. Valuable space has not been sacrificed to make room for unnecessary illustrations ; the subject matter is put clearly and with enough detail to make the description of methods and apparatus easy to understand. The section dealing with physiology has been carefully revised and gives us a useful summary of the most recent teaching with reference to surgical shock, and in this connection the reader is warned of the old fallacy of regarding deep ether anæsthesia as a safeguard. It is perhaps rather surprising that for ordinary work nitrous oxide and oxygen anæsthesia has not been given greater prominence. We feel that this edition well maintains the good tradition of its predecessors as an essentially practical and very valuable book for all interested in this somewhat complex subject. The publishers are to be congratulated upon the excellent manner in which it has been turned out.

BOOK   NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest for our readers.]

A Text-book of Surgery for Dental Students. By G. PERCIVAL MILLS, M.B., B.S. (Lond.), F.R.C.S., Hon. Surgeon, General Hospital, Birmingham, etc. ; and HUMPHREY HUMPHREYS, O.B.E., M.C., T.D., K.H.P., M.B., Ch.B., M.D.S. (Birm.), L.D.S. (Eng.), Lecturer on Dental Anatomy, Birmingham University, etc. Fourth edition. Large 8vo. Pp. 342 + xii, with 63 illustrations. 1935. London : Edward Arnold & Co. 14s. net.

The Diseases of the Endocrine Glands. By HERMANN ZONDEK, M.D. (Berlin), translated by CARL PRAUSNITZ, M.D. (Breslau), M.R.C.S., L.R.C.P., Hon. Research Fellow, Victoria University of Manchester. Large 8vo. Pp. 492 + xi, with 168 illustrations. 1935. London : Edward Arnold & Co. 40s. net.

The Principles and Practice of Urology. By FRANK HINMAN, A.B. Leland Stanford Junior University, M.D. Johns Hopkins Medical School ; Clinical Professor of Urology at the University of California Medical School. Large 8vo. Pp. 1111, with 513 illustrations. 1935. London and Philadelphia : W. B. Saunders Company. 45s. net.

Surgical Nursing and After-treatment. A Handbook for Nurses and Others. By H. C. RUTHERFORD DARLING, M.D., M.S. (Lond.), F.R.C.S. (Eng.), F.R.F.P.S. (Glasgow), Surgeon, Prince Henry Hospital, New South Wales Hospital (Langton Clinic), etc. Crown 8vo. Pp. 738 + xii, with 187 illustrations. 1935. London : J. & A. Churchill Ltd. 9s. net.

IPSISSIMA VERBA

BY SIR D'ARCY POWER, K.B.E., LONDON

VII. C. H. MOORE, F.R.C.S., AND OPERATIONS FOR CANCER

CHARLES HEWITT MOORE may be looked upon as a pioneer of the modern operation to prevent recurrence after operation for cancer of the breast and so to cure the disease.

He was born at Plymouth on June 12, 1821, the second son of William Moore, who came of a well-known ship-building family. He was educated at the Plymouth Grammar School and was sent to London to study medicine on the advice of his uncle, Dr. Joseph Moore. Here he was apprenticed to Frederick Carpenter Skey, then Assistant Surgeon at St. Bartholomew's Hospital. Skey was a seceder from the medical school of the Hospital in one of those quarrelsome periods to which the London hospitals were accustomed during the nineteenth century. Skey was lecturing at the Aldersgate School of Medicine, and in 1842 Moore helped his master with the anatomy class. During his pupilage he acted as Clinical Clerk to Sir George Burrows, and in October, 1844, he was nominated House Surgeon by John Painter Vincent. He used to say in after life that to Burrows and Skey he owed his ability to think precisely and observe with accuracy. Burrows, on his side, said that Moore was one of the best of his clinical clerks, thoughtful, painstaking, and conscientious.

Moore took out courses at Vienna and Berlin for two years after his house surgeoncy ended in October, 1845, and on his return to England in 1847 was appointed at first Demonstrator and in the following year Lecturer on Anatomy at the Middlesex Hospital, holding the post for twenty years. He was elected Assistant Surgeon to the Hospital in 1848, and within a few months was appointed full Surgeon at the age of 27. He became Lecturer on Systematic Surgery in 1869 with Campbell de Morgan as his colleague, but the promotion came too late, for he had a cerebral hæmorrhage at the end of his first course of lectures and died after a prolonged illness on June 6, 1870.

Moore was in charge of the special cancer wards at the Middlesex Hospital for many years, and on May 28, 1867, he read a paper at the Royal Medico-Chirurgical Society giving the results of his experience. It is entitled, " On the

Influence of Inadequate Operations on the Theory of Cancer ". He summarizes his conclusions in the following paragraphs, and in reading them it should be borne in mind that his contemporaries had almost given up operating upon cancer of the breast because their patients always had a recurrence within a short time. Moore says (*Med.-Chir. Trans.*, 1867, 1, 245–80) :—

" Local recurrence of cancer after operations is due to the continuous growth of fragments of the principal tumour.

" Such recurrence may take place also in a residual part of the organ respecting which it cannot be asserted that it was cancerous at the time of the operation.

" Such recurrence may further happen in a structure adjoining a completely extirpated breast and on a comparison of cases may be held to be produced by disseminated fragments of the original tumour.

" The recurrent Cancer is subject, as well as due, to local conditions and especially adapts itself to the distribution of the absorbents. Its continuity with the first tumour may be traceable over half the chest, the pleura, and the glands from the neck to the loin or the inguinal region, and possibly also to the liver.

" After the removal of a portion of the breast the recurrent Cancer does not involve the remainder of the organ indiscriminately, but commences in that part of it which immediately adjoins the scar.

" The progress of recurrent Cancer after a partial removal of the breast is not exclusively organic, and does not even show a preference for that organ, but rather is centrifugal from the scar ; and, when free in both directions, it tends toward the axilla earlier than to the residue of the breast.

" Cancer once established in either mamma, its primacy is supreme. When one breast has been wholly or partially removed, recurrent Cancer does not spring up as a new disease in the opposite breast, but on the same side as the original tumour. It may, nevertheless, be possible that a mammary Cancer having been wholly extirpated, Cancer may reappear in another part of the body, which other part may be the remaining breast. I have not met with such a case.

" It is not sufficient to remove the tumour or any portion only of the breast in which it is situated ; mammary Cancer requires the careful extirpation of the entire organ.

" The situation in which the operation is most likely to be incomplete is at the edge of the mamma next the sternum.

" When any texture adjoining the breast is involved in or even approached by the disease that texture should be removed with the breast. This observation relates especially to skin, to lymphatics, to much fat, and to pectoral muscle. The attempt to save skin which is in any degree unsound is of all errors perhaps the most pernicious, and whenever its condition is doubtful that texture should be freely removed. A broad scar, and the stretching and compression due to its subsequent contraction appear to be especially satisfactory.

" In the performance of the operation it is desirable to avoid not only cutting into the tumour, but also seeing it. No actually morbid texture should be exposed, lest the active microscopic elements in it be set free and lodge in the wound. Diseased axillary glands should be taken away by the same dissection as the breast itself, without dividing the intervening lymphatics ; and the practice of first

roughly excising the central mass of the breast, and afterwards removing successive portions which may be of doubtful soundness, should be abandoned. Only by deliberately reflecting the flaps from the whole mamma, and detaching it first at its edge, can the various undetected prolongations of the tumour and outlying nodules be included in the operation. To parts suspected of disease but not capable of removal it is desirable to apply the chloride of zinc.

" The conclusions briefly stated, are partly theoretical and partly practical. The former are :—

" That the recurrence of Cancer is due to local conditions :

CHARLES HEWITT MOORE

" That these conditions are not regional, so as to belong to structures out of continuity with the first tumour.

" That neither are they organic, whether as indiscriminately involving the residue of a mamma operated upon, or so as to be transferable to the second breast in consequence of the removal of that first affected ;

" That, on the contrary, recurrent Cancer begins near the scar ;

" That, when free in both directions, it tends toward the axilla earlier than to the residue of the breast ;

" That, consequently centrifugal dispersion, not organic origin, determines the recurrence of Cancer.

" The practical conclusions are :—

" That Cancer of the breast requires the careful extirpation of the entire organ ;

" That the situation in which this operation is most likely to be incomplete is at the edge of the mamma next the sternum,

" That, besides the breast unsound adjoining textures, especially skin, should be removed in the same mass with the principal disease."

These were hard sayings for a generation where an operation was always followed by suppuration and which looked to the cosmetic effect rather than to cure. The paper attracted so little attention that it was not thought worthy of notice by the medical journals and the discussion upon it was in the main adverse. Perhaps the personal element was a factor, for one of his contemporaries said of him that " Moore combined extreme caution with surprising rashness." It came under the notice, however, of Lister and of Mitchell Banks, who put it into practice in their own wards, and this was the beginning in England and Scotland of the modern operation for the cure of cancer.

TRAUMATIC HÆMANGIOMATOUS TUMOURS OF SKELETAL MUSCLE

By ROBERT MAILER

ASSISTANT SURGEON, VICTORIA INFIRMARY, GLASGOW

VASCULAR tumours of striated muscle constitute a rare but well-recognized and interesting group. The last comprehensive survey of the literature by Jenkins and Delaney[7] in 1932 revealed 256 authentic cases, chiefly from continental sources, though cases have been described in this country by Gibb,[6] Bland-Sutton,[1] and Wakeley.[13] To Liston[8] belongs the credit of having described the first case as early as 1843. He called it an erectile tumour of the popliteal space, and it was found to be an angioma in association with the semimembranosus muscle.

Most of the cases reported have been described as cavernous angioma or hæmangioma of muscle, though frequently the terms capillary, venous, and arterial angioma are met with according as one or other of these vascular elements appeared to dominate the pathological picture.

Considered collectively, these tumours for the most part are non-encapsulated or only partially encapsulated, and at operation present infiltrating characters suggestive of sarcoma. Yet they are benign in their behaviour and rarely recur after removal. Their occurrence almost exclusively during the first three decades of life, taken in conjunction with the usually accepted views with regard to the etiology of angiomatous tumours elsewhere in the body, has strengthened the belief that these tumours are of congenital origin. The following case, therefore, seems worthy of presentation because the clear-cut history and the pathological findings pointed definitely to trauma as the exciting agent.

CASE REPORT

P. M., male, aged 21. This patient was first seen in consultation on Dec. 11, 1934. Complaint: swelling in the arm of two months' duration.

HISTORY.—Four months previous to consultation the patient had been involved in a motor accident. The light racing car in which he was travelling turned over, and his left arm was pinned under the weight of the car. There was severe bruising over the inner side of the arm from the anterior fold of the axilla to the elbow. Considerable pain was present for about ten days. Subsequent to this there was pain on swinging the arm on walking, and it was more comfortable to hold it in the sling position. A tender area remained about the middle of the upper arm on its inner and posterior aspect. Within three weeks of receiving the injury the patient resumed his usual activities, which included the breaking-in of young horses and participation in one or two junior steeplechases. He was conscious that his left arm tired readily, though he had no actual twinges of pain except when taking jumps.

Two months before consultation he became aware of a swelling about the size of a walnut on the inner and posterior aspect of his left arm. This had increased in size up to the time of examination.

ON EXAMINATION.—There was an ovoid swelling about the size of a hen's egg on the inner and posterior aspect of the left upper arm. Its long axis was in the long axis of the arm. It was smooth, firm, and elastic in consistence. The skin overlying it was normal in appearance and freely movable. The swelling was not attached to bone. It was movable to some

extent in a transverse axis, but not in a longitudinal, and it became more prominent and fixed when the extensor muscles were tightened. Its borders were poorly defined, and it had the feeling of an infiltrating rather than an encapsulated swelling. It was slightly tender.

PROVISIONAL DIAGNOSIS.—Fibroma of triceps muscle.

In view of the history of rapid growth and the infiltrating character of the swelling, which made it impossible to exclude sarcoma, operation was advised.

OPERATION.—The triceps muscle was exposed and an infiltrating tumour mass excised from the belly of the inner head. It was necessary to sacrifice a considerable bulk of muscle to get clear of the growth. Bleeding was very free, but was readily controlled. The wound was closed without drainage. Healing was uninterrupted, and when the patient was seen three months later there was no demonstrable functional impairment of the arm.

FIG. 188 —Low-power microphotograph of angiomatous tumour showing numerous capillaries in a young connective-tissue stroma. At the upper margin the tumour is seen extending between groups of muscle fibres. (Hæmatoxylin and eosin) (× 110.)

PATHOLOGICAL REPORT.—The specimen is an ovoid mass of tissue about 6 cm. by 5 cm. with attached muscle fibres. On section there is a large central cavity with smooth wall about 1·5 cm. by 1·5 cm., containing a partially organized blood-clot. The remaining tissue sectioned is yellowish-white or greyish-white in colour, fairly firm nearer the central cavity, but softer nearer the periphery.

Microscopic Examination.—The area immediately surrounding the central cavity consists of organizing fibrin with clumps of red blood-cells in a matrix of young fibrous connective tissue. One or two fragments of degenerated muscle fibre are still recognizable. Sections of the peripheral portion of the tumour show an enormous vascular overgrowth involving chiefly capillaries (*Fig.* 188), but also in areas a very extensive overgrowth of the smaller muscle-walled arteries is seen (*Fig.* 189). These arteries have thickened walls, and some of

them contain thrombi. Here and there are large irregular vascular spaces of the cavernous type. These are lined by a single layer of endothelial cells and have a wall of fibrous connective tissue.

These vascular elements are found in a loose fibrous connective-tissue stroma. Capillary hæmorrhages are frequent in the border zone between tumour and intact muscle fibres (*Fig.* 190). The angiomatous formation is seen extending between muscle fibres or groups of muscle fibres. The latter are in various phases of degeneration (*Fig.* 191). Some fibres show only a loss of staining reaction; others show their sarcoplasm shrunken and fragmented, while in adjacent areas the fibres have disappeared and are replaced by a hyaline matrix suggestive of the Zenker type of coagulation necrosis. A few fibres show proliferation

FIG. 189.—Low-power microphotograph showing in addition to numerous capillaries arterioles with thickened walls. (Hæmatoxylin and eosin.) (× 110.)

of sarcolemma nuclei and the formation of 'muscle tubes' such as have been described by Waldeyer,[14] Weber,[15] Dawson[14] and others in their studies in muscle regeneration. The vascular overgrowth always follows the endomysial trabeculæ and never penetrates the sarcolemma of the muscle fibre. There is no encapsulation anywhere.

PATHOLOGICAL DIAGNOSIS.—Mixed capillary and arterial angioma.

A SHORT SURVEY OF THE LITERATURE

A study of the 256 cases reported in the literature shows that while angiomatous tumours of muscle may vary widely as regards size, consistency, rate of growth, etc., there are certain features common to the majority. These are summarized below.

Age Incidence.—Of the reported cases 80 per cent occurred before the age of 20, and 95 per cent before the age of 30, so that they are tumours of childhood or early adult life.

Situation of the Tumour.—The lower extremity was the most common site, especially the thigh (107 cases). The quadriceps extensor was the muscle most frequently involved. The upper extremity, especially the biceps and triceps muscles, accounted for 64 cases.

Clinical Features.—A tumour mass, round or ovoid, varying in size from a nut to an egg, growing slowly and at first painlessly, was the common finding.
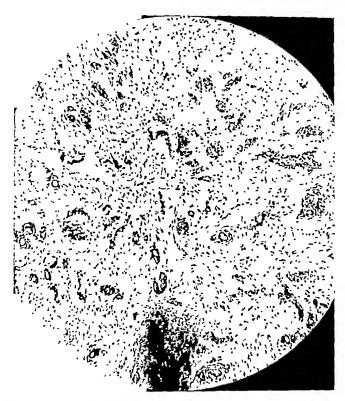
FIG. 190.—Low-power microphotograph showing numerous capillaries with proliferative changes round the walls. A hæmorrhage is also seen in the lower part of the section. (Hæmatoxylin and eosin.) (× 110.)

The tumour was usually diffuse and often tender. The consistency varied: in 64 cases it was described as soft, but in 55 cases it was hard, and in 30 elastic. Sometimes it could be reduced in size by pressure or by elevating the limb. The overlying skin was almost invariably normal in appearance and freely movable over the tumour. Pain usually developed at some time in the course of the disease. Some functional impairment was frequently present when the tumour was situated in an extremity, and not uncommonly there was actual deformity.

Diagnosis.—This was made previous to operation in only 21 cases. In soft semi-fluctuant tumours resembling abscess, the diagnosis was made by the exploring needle withdrawing blood. Occasionally an X-ray photograph demonstrated phleboliths as in Wakeley's case.

Pathological Features.—The tumour in section was often described as bluish or reddish, but sometimes as greyish or yellowish-white. Blood cysts were noted in five cases, and sometimes nodular areas due to phleboliths.

Under the microscope the tumour was described as made up of vascular elements in a connective-tissue stroma. The most frequent vascular formation was the cavernous space. Arterioles with thickened walls were often present, and often capillaries. The latter were sometimes the predominating feature. Thrombi in

FIG. 191.—Low-power microphotograph of degenerating muscle fibres showing change in staining reaction and proliferation of sarcolemma nuclei. The angiomatous formation is seen extending between the groups of degenerating fibres. (Hæmatoxylin and eosin.) (× 110.)

varying stages of organization were frequently present in the lacunæ or large vessels. The stroma varies in its cellular elements, and in six cases the possibility of sarcoma was considered, the fibroblastic proliferation being so marked. Round-celled accumulations were often present. In the stroma were remnants of striated muscle in some stage of degeneration. In the central part of the tumour the degenerative changes were usually complete, but towards the periphery the fibres were better preserved and even apparently normal.

Etiology.—There has been some difference of opinion between pathologists as to whether angiomata constitute true neoplasms. Ribbert[10] favoured the Cohnheim theory that angiomata develop from embryonic rests. Virchow[12] suggested that these tumours arose from the effect of local irritation on imperfectly

formed blood-vessels. On the other hand, Rokitansky[11] considered that they represented a simple hypertrophy of the vascular elements and not a neoplastic overgrowth. Trauma as a factor has been stressed by Lowenthal and Pilzer.[9]

In the 256 cases of muscle angioma reviewed in the literature trauma was mentioned as a possible factor in 43 (17 per cent). Yet the early age incidence has inclined most authors to regard the congenital factor as of supreme importance, with trauma as an occasional secondary exciting agent.

DISCUSSION

In the case reported here there is no doubt that trauma was the etiological factor at work. The clear-cut history and the pathological appearance of the tumour with central organizing blood-clot allows of no other explanation. Angiomatous tumours, apart from the vascular nævus, are not common in any situation, and their occurrence relatively often in muscle suggests something more than a developmental factor. Skeletal muscle is exposed not only to external trauma, but also to trauma dependent upon its inherent contractile power. Cases of complete rupture of muscle due to strong muscular contraction are occasionally met with, especially in the biceps, quadriceps, and rectus abdominis. Such cases call for immediate operative treatment, and as far as I am aware are never followed by tumour overgrowth. Again, one of the commonest causes of injury to muscle is a fractured bone, yet angiomatous formations in muscle following fracture are not met with. In the case of complete rupture of muscle, and also in association with injury due to fracture, rest and immobilization are ensured. It is, however, with minor traumata of muscles that conditions may be different. Here a few fibres only may be torn. A blood-clot forms and the torn fibres retract. Granulation tissue fills the gap, and this may be modified by several factors. In the first place muscle fibres have a limited power of regeneration, and this is more manifest in younger subjects. The exciting agent in the reactive processes is a substance furnished by the bruised muscle fibres, and Dawson[4] has pointed out in his studies on muscle repair that the endothelial proliferation is most intense. Though it is impossible for muscular tissue to regenerate and bridge a gap of more than 3 or 4 mm. under the most favourable conditions, it appears reasonable to suppose that the reactive processes develop on a scale commensurate with this possibility. The relatively large blood-clot due to the retraction of torn muscle fibres also offers a most favourable medium for excessive cell proliferation. This might reasonably explain the angiomatous nature of the granulation tissue, but it does not offer an explanation of the infiltrating nature of the process and the absence of self-limitation. This, however, can be explained on the basis of the repeated traumata to which the young vascular granulation tissue is exposed owing to muscular contraction. Capillary hæmorrhages develop. Muscle fibres at the periphery of the tumour are separated, damaged, and undergo degeneration and the cycle of reactive changes is repeated. On this basis the tumour is to be regarded more correctly as a soft non-encapsulated fibroma showing special angiomatous features dependent on its situation in highly specialized contractile tissue, damage to which is associated with a more intense endothelial proliferation than is met with in any other tissue. Moreover, this highly vascularized tissue in virtue of its situation in muscle cannot fail to be subjected to strains, resulting in hæmorrhages, which account for the progressive enlargement.

It is not contended that from a study of a single case one can generalize on the etiology of these tumours. They do not all conform to the same type, and in some a simple saccular and tubular dilatation of pre-existing veins would seem to explain their origin. For example, the angioma of the gracilis muscle removed by Stonham[2] and now in the Westminster Hospital Museum resembles a widespread varix. On the other hand, from a study of the case presented here, together with the reports of many similar cases in the literature, there are reasonable grounds for supposing that trauma is the important factor in their development and that there is no necessity for postulating a congenital factor universally. Some cases occurring in new-born children would appear almost certainly to be congenital, though here again birth injuries might have to be considered. Lastly, on this hypothesis, the occurrence of these tumours in young subjects is explainable on the basis that the latter are more exposed to trauma, together with the fact that the younger the patient the greater the potentiality and the intensity of the regenerative process.

SUMMARY

A case of hæmangioma of the triceps muscle in a man of 21 is described. The tumour was non-encapsulated, and consisted of dilated capillaries and thick-walled arterioles in a young fibrous connective-tissue stroma. The history and pathological appearances afforded strong evidence that the tumour was traumatic in origin. A short survey of the 256 cases previously reported in the literature is appended, and the importance of the traumatic factor as against the congenital factor is stressed. Based on a study of the present case, an explanation is given how trauma acts in the production of these hæmangiomata of muscle.

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TWO CASES OF HÆMANGIOMA OF VOLUNTARY MUSCLE: WITH A BRIEF REVIEW OF THE LITERATURE

E. N. MacDERMOTT

PROFESSOR OF THERAPEUTICS, PHARMACOLOGY, AND MATERIA MEDICA, UNIVERSITY COLLEGE, GALWAY
HON. SURGEON, CENTRAL HOSPITAL, GALWAY

IN view of the rarity of these tumours the following two cases seem worthy of report.

Case 1.—Unmarried woman, aged 24. First seen in October, 1932, complaining of pain and swelling of the left leg. She had been in hospital seven years previously, when 'varicose veins' had been removed from the left calf; and again in 1929, when she had been unavailingly treated by massage for the same pain and swelling. The calf was swollen fairly uniformly for about 2 in. below the line of the knee-joint to about $1\frac{1}{2}$ in. above the ankle; the two scars of the varicose vein excision were visible on the back of the calf; the limb was neither œdematous nor tender. An area of greater resistance suggesting a calcified plaque or fibrous node about the size of a florin could be felt on the inner side of the calf around the centre. There was no abnormality in any of the limb bones, and the X-ray taken during her last visit to hospital was negative.

A provisional diagnosis of pseudo-elephantiasis or muscle angioma was made and exploratory operation advised.

OPERATION.—This was done under general anæsthesia. An incision about 2 in. long was made over the palpable mass down to the deep fascia. Here was found a thickened area of fascia surrounded by thin-walled dilated veins. The deep fascia was opened and a mass of fibro-fatty and angiomatous nature revealed between the deep and superficial muscles, and partly infiltrating the latter. The tumour readily shelled out except where it had infiltrated the soleus, which was extensively replaced by tumour tissue, and the gastrocnemius, which was only slightly involved. To expose the mass it was necessary to extend the incision to $\frac{1}{2}$ in. behind the internal malleolus below, and $\frac{1}{2}$ in. below the line of the knee-joint above. The mass extended above almost right across the leg, leaving very little normal soleus outside it, while below it tapered to about the thickness of the little finger and was easily shelled out from the connective tissue. The muscle adjacent to the palpable edge of the tumour was yellowish and not contractile. The tumour was removed by enucleation where possible, and cutting through healthy, contractile muscle where no line of cleavage was evident. The muscles were reconstituted as well as possible and the wound was sutured, a rubber-dam drain being left beneath the deep fascia. Convalescence was quite uneventful.

I had an opportunity of re-examining this patient last August, over twenty months after operation; there is nothing to suggest recurrence, and the muscle of the calf has hypertrophied so that there is no significant difference in the circumference of the two legs.

PATHOLOGY.—After preservation in alcohol the specimen measured $9\frac{1}{2}$ in. in length and $2\frac{1}{2}$ in. at its widest part. To the naked eye it appeared to be for the most part fibro-fatty tissue, well encapsuled, with areas of dilated vessels most numerous towards the margin of the tumour where it was infiltrating the muscle. Microscopically these observations were confirmed; the vascular areas were typically angiomatous in structure. Where the tumour was invading the muscles, the endothelial cells were especially numerous, and the adjacent muscle fibres were degenerated, appearing relatively opaque and having lost their transverse striation. The tumour seemed to have a more vascular spreading margin which destroyed, and then replaced, the muscle, and was in its turn replaced by fibro-fatty tissue containing angiomatous islets. Unfortunately the original slides were thrown out in the pathological laboratory, and as the tumour had been hardened in alcohol for such a long time it was not possible to prepare a second set of slides for microphotographs.

Case 2.—Boy, aged 12 years. About three years previously his mother noticed a swelling about the centre of the dorsal region to the right of the middle line : he was admitted to a hospital, where a tentative diagnosis of Pott's caries was made. Three aspirations of the mass yielded only blood, and his X-ray showed no bony changes ; he was seen by several practitioners and ultimately provided with a spinal jacket, which he had worn for over two years, when he was referred to me by the T.B.M.O. He presented then a swelling the size of a duck's egg in the mid-dorsal region just to the right of the middle line and apparently in the erector spinæ. His mother stated that the mass had increased only slightly in size in the preceding two years. The skin over the swelling looked normal and was not adherent ;

the mass was resilient, well-defined, and irreducible, and dull on percussion ; no sounds were heard on auscultation over it ; there was no clinical evidence of Pott's disease. On aspiration pure blood was obtained.

A provisional diagnosis of hæmangioma of the erector spinæ was made, though the alternatives of sarcoma, spinal caries, and hernia pulmonis were not absolutely excluded.

OPERATION.—Under ether anæsthesia an incision was made over the mass and the dorsal fascia opened ; a whitish mass not adherent to the fascia was exposed. This was easily shelled out from the erector spinæ at the sides, but there was no line of demarcation between tumour and muscle above and below, thus necessitating removal of some muscle with the growth. As in *Case* 1, the wound was closed with a small dam drain and convalescence was uneventful.

I saw this boy seventeen months after operation and found his back perfectly healthy.

PATHOLOGY.—The tumour was about the size of a duck's egg and greyish-white in colour ; on section it showed numerous purplish islets about $\frac{3}{8}$ in. in diameter. Microscopically these islets were

FIG. 192.—Microscopical appearance of muscle angioma.

seen to be composed of large blood-spaces with an endothelial lining, and rather loose fibrous tissue ; the remainder of the tumour consisted of less vascular tissue with a more dense connective-tissue stroma (*Fig.* 192). The tumour was therefore a fibro-hæmangioma.

DISCUSSION

Hæmangioma of muscle was first described by Muscatello (1894). A closely detailed review of the cases reported up to date was given by Jenkins and Delaney (1932) ; at the time their paper was written 256 such tumours had been described. I have been able to find references to two further cases by Rocher and Uzac (1931), and Truesdell (1931), bringing the number of muscle angiomata described up to

260. (This does not include cases described by Bartoli (1932), as his paper was unfortunately inaccessible to me.)

Clinical Signs.—The main signs evidenced by such tumours are: a mass usually demonstrably adherent to the muscle, though this may be masked by the overlying soft tissues; the mass is of varying consistence, depending on the proportion between fibrous tissue and vessel spaces, from moderately firm to so fluctuant as to support the diagnosis of abscess, though the tumour is only rarely adherent to the skin. *On aspiration blood is obtained, but this per se does* not exclude sarcoma or cyst from the diagnosis. Radiologically phleboliths were found in 34 cases out of 63 so examined (they were not found in my two cases, both of which had been radiographed before they were seen by me).

Other symptoms described are in approximate order of frequency: (1) *Pain*, which may be constant but is generally increased on exertion; (2) *Limitation of movement* due to mechanical interference by the tumour mass; (3) *Loss of function* or *deformity* due to the replacement of muscle tissue by the angioma, as in *Case* 1; (4) *Pressure symptoms* due to pressure on vessels or nerves causing (*a*) hypertrophy of a limb, (*b*) anæmic atrophy, (*c*) diminished pulsation in the vessels distal to the lesion, or (*d*) referred pain; (5) Rarely the skin has been described as *bluish* in colour (seven cases) or *containing dilated veins* (five cases and *Case* 1); (6) *Calcification* of part of the tumour was noted in four cases, and *pulsation* in four others; (7) A *buzzing* sound on auscultation was described in one case; (8) X-rays give mainly negative information, though the finding of *phleboliths* in a suspicious case renders more probable the diagnosis of angioma.

Diagnosis.—On surveying the literature one is struck by the rarity of correct diagnosis of these tumours; a correct pre-operative diagnosis was made in only 12 per cent, while it was only considered as an alternative diagnosis in 2½ per cent, including my two cases. Such growths must often escape recognition owing to the regrettable disuse into which exploratory incision has been pushed by perhaps excessive reliance on radiological and laboratory aids to diagnosis.

Table I gives a survey of the diagnoses: (1) In the 91 cases in which a definite pre-operative diagnosis was made; and (2) In the 34 cases in which an alternative diagnosis was made. In many of the reported cases no pre-operative diagnosis was mentioned.

Table I.—PRE-OPERATIVE DIAGNOSIS

	DEFINITE	ALTERNATIVE		DEFINITE	ALTERNATIVE
Abscess, acute	1	—	Lipoma	11	4
Abscess, chronic ..	6	3	Myoma	2	—
Aneurysm	1	—	Myositis	1	1
Angioma	31	6	Neoplasm, benign ..	4	2
Angiofibroma ..	1	—	Neoplasm, malignant ..	2	—
Angiolipoma ..	1	—	Neuroma, false ..	1	—
Angiolymphoma ..	4	—	Neuroma, true	5	1
Arthritis	1	2	Osteomyelitis	2	1
Bone tumour ..	1	—	Pelvic cellulitis ..	1	—
Bursitis	1	—	Phlebitis	1	—
Club-foot	1	—	Sarcoma	2	3
Cyst (including dermoid)	7	6	Synovitis	—	1
Epithelioma	1	—	Tuberculosis of muscle	1	1
Ganglion	1	—	Tuberculous glands ..	1	—
Gumma	1	2	Tuberculous spine ..	1*	—
Hernia, epigastric ..	—	1	Varix	2†	—
Hernia, parumbilical ..	1	—			

* Case 2.   † Including Case 1.

Pathology.—The noteworthy points in the pathology of these tumours are : (1) That while clinically benign, metastases never occurring and recurrence being very rare (and then most probably due to incomplete removal), they may exhibit a peculiar local malignancy, infiltrating the muscle, which degenerates before them ; and (2) The tendency towards partial replacement of the originally angiomatous structure by fibrous or fatty tissue in the centre.

Table II shows distribution as gleaned from a study of the literature.

Table II.—MUSCULAR DISTRIBUTION OF ANGIOMATA ACCORDING TO REGIONS

Head—	
Temporal 3	Flexor carpi ulnaris 3
Masseter 15	Pronator radii teres 3
Orbicularis oculi 2	Pronator radii quadratus 1
Rectus internus 1	Extensor carpi radialis longus.. .. 1
Inferior oblique 11	Extensor carpi radialis brevis.. .. 1
Buccinator 1	Extensor longus pollicis 2
Neck—	Extensor carpi ulnaris 2
Splenius 1	Supinator longus 5
Sternomastoid 4	Thenar muscles 8
Depressors of tongue and lower jaw.. 1	Hypothenar muscles 3
Chest—	*Lower Limb—*
Intercostals 2	Ilio-psoas 2
Abdomen—	Gluteus maximus 5
General 4	Gluteus minimus 2
External oblique 3	Gluteus medius 4
Internal oblique 1	Gemelli 2
Rectus 6	Quadriceps 19
Back—	Vastus internus 17
Erector spinæ 10	Vastus externus 5
Quadratus lumborum 6	Crureus .. .. —
Sacrospinalis 1	Rectus femoris 6
Upper Limb—	Sartorius 2
Trapezius 11	Adductor longus 1
Latissimus dorsi 13	Semimembranosus 10
Serratus posterior inferior 3	Semitendinosus 5
Rhomboideus major 1	Gracilis 3
Rhomboideus minor 2	Biceps femoris 12
Infraspinatus 2	Soleus 11
Pectoralis major 8	Gastrocnemius 21
Serratus magnus 5	Tibialis posticus 1
Deltoid 7	Flexor longus digitorum 3
Teres major 2	Flexor longus hallucis 4
Subscapularis 1	Tibialis anticus 2
Coraco-brachialis 1	Extensor longus digitorum 1
Biceps 7	Extensor brevis digitorum 1
Brachialis anticus 1	Extensor longus hallucis 1
Triceps 16	Extensor brevis hallucis 1
Anconeus 1	Peroneus longus 1
Flexor-pronator group 5	Peroneus brevis 2
Flexor sublimis digitorum 7	Peroneus tertius 1
Flexor profundus digitorum .. .. —	Plantaris 1
Flexor longus pollicis 2	Sole muscles 3
Flexor carpi radialis 6	*Tongue* 2

INSUFFICIENTLY LOCALIZED

Forearm 4	Arm and hand 1
Lower limb 1	Foot and leg 1
Upper limb 1	Thigh 1
Deep neck muscles 1	Leg 1

It would appear from a study of *Table II* that no muscle or muscle group is

per se especially liable to angioma, but that predominance of these tumours as reported in any particular region is explicable by the actual mass of muscle and its accessibility for examination.

Age Distribution and Recurrence.—The age distribution is shown in *Table III.*—

Table III.—AGE DISTRIBUTION OF ANGIOMA OF MUSCLES

AGES				CASES
0– 5	..	..	..	7
6–10	..	..	..	15
11–15	..	..	..	24
16–20	..	..	..	35
21–25	..	..	..	31
26–30	..	..	..	12
31–35	..	..	..	8
36–40	..	..	..	4
41–45	..	..	..	4
46–50	..	..	..	2
51–55	..	..	..	1
66–70	..	..	..	3

It is thus seen that these are growths of early life, $62\frac{1}{2}$ per cent occurring between 11 and 26 years of age.

The recurrence rate as found in the literature works out at 6 per cent, but this is usually, if not always, explicable by inadequate excision. My two cases are free from recurrence over two years after operation.

Treatment.—The obvious treatment is excision, a small margin of muscle being removed if the tumour does not shell out readily. Ligation of vessels, X rays, radium, and injection of sclerosing solutions have all been utilized, but are in general inefficacious.

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THE HISTORY OF PLASTER-OF-PARIS IN THE TREATMENT OF FRACTURES

BY J. K. MONRO

PROFESSOR OF SURGERY, KING EDWARD VII COLLEGE OF MEDICINE, AND SURGEON, GENERAL HOSPITAL, SINGAPORE

A THOUSAND years before Joseph became Governor under Pharaoh the Egyptians were using stiffened linen for splinting. It is probable that embalmer's bandage was linen, and gum or plaster the stiffening agent.[1-3]

Hippocrates,[4] who wrote about 350 B.C., used bandages " smeared with cerate and rosin " for fractures of the lower limb.

Two strong men will suffice by making extension and counter-extension. Extension must naturally be made straight in a line with the leg and thigh, whether on account of fracture of the bones of the leg or of the thigh. And in both cases they are to be bandaged while in a state of extension.

You should apply the bandages while the limb is in a stretched position . . . and the end of the bandage should be placed over the fracture . . . the bandages would be broader and larger and more numerous in the case of the leg than in that of the arm. And when it is bandaged it should be laid upon some smooth and soft object, so that it may not be distorted to the one side or the other, and that there may be no protrusion of the bones either forwards or backwards, for this purpose nothing is more convenient than a cushion.

When the thigh-bone is broken, particular pains should be taken with regard to the extension that it may not be insufficient, for when excessive, no great harm results from it. For, if one should bandage a limb while the extremities of the bone are separated to a distance from one another by the force of the extension, the bandaging will not keep them separate, and so the bones will come together again as soon as the persons stretching it let go their hold for the fleshy parts being thick and strong, are more powerful than the bandaging.

To fractures of the nose[5] he applied a waxed compress of wheaten flour, to which manna of frankincense or gum might be added.

Rhazes,[6] an Arabian physician born A.D. 860, tells of an improvement.

But if thou make thine apparatus with lime and white of egg it will be much handsomer and still more useful ; in fact, it will become as hard as stone and will not need to be removed until the healing is complete.

The practice of the Middle Ages, however, rather followed Hippocrates, and bandages stiffened by dipping in egg albumen and solidifying pastes were used. In England the method was popularized by William Cheselden,[7] surgeon and anatomist, who lived from 1688 to 1752. In his *Anatomy of the Human Body* he wrote :—

I thought of a much better bandage, which I had learnt from Mr. Cowper, a bone-setter at Leicester, who set and cured a fracture of my own cubit when I was a boy at school. His way was, after putting the limb in a proper posture, to wrap it up in rags dipped in the whites of eggs, and a little wheat flour mixed ; this drying, grew stiff, and kept the limb in good posture. And I think there is no way better than this in fractures, for it preserves the position of the limb without strict bandage, which is the common cause of mischief in fractures.

The functional result in Cheselden's own arm[8] was evidently excellent, for, in younger days he was a keen boxer, and at the height of his professional career his

manual dexterity was such that he completed the operation of cutting for stone in sixty-eight seconds. Cheselden recommends making the apparatus thin over the crest of the tibia " so as to facilitate cutting it up and tightening it when it becomes loose ". A picture of the apparatus is reproduced in the *Robert Jones Birthday Volume*.[9] Sixteen years later Le Dran[10] introduced similar methods in France, stiffening his apparatus with white of egg, vinegar, and powder of Armenian bole (an earthy mineral resembling clay), or with starch or plaster. Percivall Pott,[11] in his *Remarks on Fractures* (1769), makes no mention of any hardening dressing, but enunciates an important principle when he insists that in splinting fractures the joint above and the joint below the fracture must be immobilized. He advises that dressings and splints be applied firmly about joints but loosely over the fracture.

Meanwhile in Arabia the use of plaster-of-Paris had probably continued with little change. This was made known in Europe by Mr. Eton,[12] who had been British Consul in Bassora. In 1798 he published *A Survey of the Turkish Empire*, in which there is the following interesting reference to the treatment of fractures.

I saw in the eastern parts of the Empire a method of setting bones practised, which appears to me worthy of the attention of surgeons in Europe. It is by inclosing the broken limb, after the bones are put in their places, in a case of plaster-of-Paris (or gypsum) which takes exactly the form of the limb, without any pressure, and in a few minutes the mass is solid and strong. . . . This substance may be easily cut with a knife, and removed, and replaced with another. If, when the swelling subsides the cavity is too large for the limb, a hole or holes being left, liquid gypsum plaster may be poured in, which will perfectly fill up the void, and exactly fit the limb. A hole may be made at first by placing an oiled cork or bit of wood against any part where it is required, and when the plaster is set, it is to be removed. There is nothing in gypsum injurious, if it be free from lime ; it will soon become very dry and light, and the limb may be bathed with spirits, which will penetrate through the covering. I saw a case of a most terrible compound fracture of the leg and thigh, by the fall of a cannon, cured in this manner. The person was seated on the ground, and the plaster case extended from below the heel to the upper part of his thigh, whence a bandage, fastened into the plaster, went round his body.

A similar method, perhaps as ancient, was in use in India. Sir George Ballingall[13] tells :—

The practice of enveloping fractured limbs in splints and bandages, without undoing them for weeks together, is akin to that followed by the natives of India, of inclosing fractured limbs in moulds of clay. Of the successful result of this practice I remember a remarkable instance in the case of a little boy who was brought into my tent one morning, having been run over by a waggon on the line of march, and having sustained a severe compound fracture of the leg. I was preparing to amputate this boy's limb when his parents came in and carried him away to the potter in an adjoining village, who enveloped the leg in clay, and I believe finally cured the patient.

Napoleon's surgeon, Baron Larrey, in the Egyptian campaign of 1798, used fixing agents of the Cheselden kind in his " appareil inamovible.[14]

This apparatus consisted of many-tailed bandages ; of roller bandages impregnated with a hardening liquid made of a mixture of camphorated alcohol, lead lotion and white of egg in water—these wrapped round the limb ; and strips of leather ; of two cylinders of straw sewn strongly with string and serving as packing, etc. ; the whole being saturated with the hardening fluid. This bandage becomes hard as it dries, and is left in place until healing occurs, unless there is some grave complication.

Hubenthal[15] (1816) used equal parts of plaster-of-Paris and ground-up blotting paper. He greased the limb to prevent the plaster adhering to it and split the plaster down the sides, making the anterior and posterior halves interlock in rather

an ingenious way. With a spatula he spread his mixture over the posterior part of the limb and trimmed the edges of this half-mould while still soft, and cut notches in it. He next greased this serrated edge and proceeded to make the anterior half-mould. He adapted the method also to fractures of the upper limb, and even to those of the clavicle.

In 1828 Koyl and Kluge, followed by Dieffenbach, attempted to generalize the use of plaster-of-Paris at the Charité Hospital in Berlin. Their method was to rest the limb in a wooden box, into which liquid plaster-of-Paris was then poured until the limb was almost, but not quite, covered. This allowed the fracture site to be kept under observation without detracting from the solidity of the plaster. When the plaster had set, the wooden box was removed, for its sides were fixed together merely with hooks, while its inner side was greased. Dieffenbach applied plaster only when the swelling had subsided. This " plâtre coulé " method closely resembles that of the Arabian physicians described above.

The use of gums and pastes was brought to its greatest perfection in Brussels by Seutin, Senior Medical Officer of the Belgian Army about 1834, and this method remained the most popular until the establishment of the plaster-of-Paris bandages. Seutin's writings are rather spoiled by an undercurrent of controversy. He is at great pains to establish his claim to having invented the method. Plagiarism is the charge made against M. Velpeau, of Paris, who made a small modification in the technique by substituting dextrin for starch. But full recognition of Seutin's originality was made in a letter written by Velpeau in 1837 and reprinted in Seutin's book. In fact, Seutin claimed originality for several features that had been used previously—for example, the splitting of the case down the front for inspection of the limb and for tightening the plaster. Such inspection dates from the Arabians, the tightening from Cheselden. Later Seutin stressed his contention that plaster-of-Paris was a poor substitute for his " bandage amidonné ".

He did, however, make a great advance in appreciating the disadvantage the patient suffered by being confined to bed throughout the period of healing.

On n'avait pas encore bien compris que l'immobilité du corps, tant recommandée par les auteurs comme auxiliaire des autres moyens curatifs, n'est qu'un véritable pis-aller qu'il faut plutôt éviter que prescrire ; on n'avait pas encore osé dire que la consolidation de la rupture osseuse est d'autant plus sure et prompte que le blessé se livre a plus de mouvements, et oublie, pour ainsi dire, son affection pour reprendre une partie de ses occupations ordinaires.

La déambulation ne peut occasionner ni accident ni déplacement des fragments : . . . en permettant au malade de se distraire de se retremper au grand air, au lieu de rester cloué sur son lit, elle a la plus heureuse influence sur la formation et la consolidation du cal.

With Cheselden's, Larrey's, or Dieffenbach's apparatus it was not possible for the patient to leave his bed. Seutin's book has a picture of a man whose fractured leg is protected by a light, strong appliance of starch bandages and kept clear of the ground by a strap round his neck ; he is going about on crutches and the sound leg, the foot of which wears a high boot.

This book gives details of Seutin's technique. The deformity was reduced and then the limb fixed as follows. The bony prominences were padded with wool, and then a roller bandage was methodically and firmly applied to cover the limb, reverses and creases being avoided. Over this, bandages soaked in starch were wound, with a cardboard splint, softened by wetting, incorporated on each side of the limb. The digits were left projecting from the apparatus so that interference

with the blood-supply by pressure could be detected. The bandages were applied firmly, rather to prevent swelling of the limb than actually to compress it.

When the cast had fully hardened it was split down the front, so that it could be hinged open throughout its whole length. For doing this he introduced a special pair of scissors, which to-day appears in instrument-makers' catalogues as 'Seutin's plaster scissors'—a deviation to a use which the originator would have condemned. If the limb was found to be in satisfactory condition, the case was re-united by a starch bandage; if it had become loose owing to subsidence of swelling, a strip beside the slit was first excised. If the limb required much local treatment, the cast could be split posteriorly as well, so as to be converted into two lateral halves, or, if the damaged part could be better approached that way, the splits could be made down the sides, so as to make an anterior and a posterior half. If the joints included in the cast tended to become stiff after long fixation, the case was temporarily removed and movements were performed while the limb was carefully held by assistants. To such an apparatus he gave the cumbrous name of 'amovo-inamovible', meaning that the apparatus when it had hardened was immovable, but that after splitting it could be temporarily removed to allow treatment of joints and soft parts. In fractures of the upper limb the patient was never confined to bed unless there was some grave complication. In the lower limb, the patient got up on crutches after the third day. The great disadvantage of the starch apparatus was that it took about two days to harden. During this time Seutin assured its rigidity by 'atelles de précaution' fixed over it. He was looking for a substance which would cause the bandage to solidify instantaneously, "persuadé d'ailleurs que tôt ou tard on parviendrait à cette découverte, qui du reste ne changerait rien aux principes de ma méthode". But plaster-of-Paris did not commend itself to him for this purpose.

In 1852 Matthysen,[16] a medical officer in the Dutch Army, published a pamphlet on the use of plaster-of-Paris for treating fractures. The finely-powdered plaster, he writes, is rubbed with the hand into strips of coarse-meshed cotton material lying on a table. The strips are then loosely rolled into bandages. He insists particularly that the cotton must be entirely free from starch and dressing, which substances retard setting, a precaution which subsequent users of plaster bandages have not always observed. He tells that his method was invented especially for convenient ('cito, tuto, ac jucunde') treatment of wounded on the battlefield, where a shortage of water for soaking the bandages might if necessary be met by using urine. The bandages were used in exactly the same way as Seutin's starch bandages, and the patient went about on crutches. Removal of the plaster was effected by wetting it and unwinding the constituent bandages. The technique was much advanced by its extensive use in the Crimean War both by the surgeons of the allied armies, and by the Russians.

In 1872 Samuel St. John[17] put forward very strongly the advantages of plaster. The splint, he writes, is fitted to the limb, and not the limb to a particular splint. It should be left undisturbed until union has occurred. Its disadvantage is that its application requires special skill if complications such as pressure sores and gangrene due to vascular obstruction are to be avoided. A great safeguard is to cut the wet plaster down the front with a shoemaker's knife. Between the skin and the plaster he placed a layer of cotton wadding or a single thickness of soft blanket. He tells that in the Franco-Prussian War the Germans used this method extensively,

employing tarlatan with plaster rubbed into its meshes, and wooden ribbons placed longitudinally between the layers of the splint to reinforce it.

In all this discussion of fracture treatment there has been little reference to the condition of the parts of the limb other than the fractured bone. Hippocrates used massage, but his successors so neglected the soft parts that stiffness was thought to be the inevitable result of immobilizing a fracture. Samuel Cooper,[18] one of the surgeons of his Majesty's Forces, wrote in 1818 :—

All fractures, however simple and well treated they may be, are constantly followed by weakness and stiffness of the limb. These unpleasant consequences are the greater, the more violently the limb has been contused, the nearer the fracture is to a joint, and the longer the part has remained motionless, and without exercise. The stiffness always affects the inferior joint of the broken bone, much more than the superior. For the relief of these effects of fractures, it is customary to employ friction, liniments, emollient relaxing applications, cold washes and bathing; but sometimes, notwithstanding such remedies, the member does not quickly recover its strength, but continues stiff and weak for a year, or even a longer time. The most effectual plans for the prevention of this state should therefore be resorted to early. These consist in making the joints, nearest the fracture, execute slight motions, as soon as the union is sufficiently advanced, not to be in danger of interruption from this practice. A great deal of caution, however, is necessary in moving the part, and it is safer for the surgeon to superintend the business himself, than leave it to the patient or others. One of the best proceedings also for the hindrance of much weakness and stiffness in the limb after a fracture is to discontinue the splints and tight bandages immediately the state of the callus will allow.

Seutin's amovo-inamovible method was designed to allow local applications to the injured limb, of whose tendency to stiffness he was well aware. John Hilton's lectures,[19] first published in 1863, refer rather contemptuously to a masseur and dub him ' rubber '. Though they make little reference to fractures, there can be no doubt that the fervour with which they preached rest must have influenced fracture treatment.[20] Hilton describes the treatment of a complete dislocation of the knee by reduction of the deformity and fixation by a starch bandage.

Sir James Paget,[21] writing of "cases that bone-setters cure", says :—

With rest too long maintained a joint becomes or remains stiff and weak and over-sensitive, even though there be no morbid process in it; and this mischief is increased if the joint have been too long bandaged, and still more if it have been treated with the cold douche. I need hardly say that it may be sometimes difficult to decide the time at which rest, after having been highly beneficial, may become injurious.

Lucas-Championnière[22] carried the idea of attention to the soft parts further. He considered a moderate degree of deformity a reasonable price to pay for absence of stiffness in a limb.

Le retour du membre au maximum possible de puissance musculaire, au maximum possible de souplesse articulaire est cent fois plus intéressant que la forme exacte du squelette.

In 1879 he condemned the prolonged immobilization which was in such universal use; and he was consequently accused of having a phobia of ankylosis, being almost alone in holding these views. He also affirmed that callus-formation and union occur best when a regulated amount of movement is allowed, quoting experiments in which movements were allowed to animals whose limbs had been fractured. This hastened union and greatly increased the amount of callus, especially in young animals, where ' de véritables tumeurs osseuses ' appeared. In children, owing to the activity of repair, movement should not be overdone, or excessive callus might cause inconvenience. In them massage is not needed, for

it exaggerates a process which is already perfectly sufficient. Immobilization, on the other hand, so interferes with the nutrition of bone that after two months there is a liability to spontaneous fracture. He quoted Ducroquet's observation that considerable force may safely be used in reducing a congenital dislocation of the hip-joint, but that, when the child has been months in plaster, a small clumsy movement may fracture the femur. If the limb is left free for a month, however, it regains its resistance to trauma. Lucas-Championnière found that surgeons had such belief in immobilization that they were reluctant to attribute this fragility to it, and preferred to postulate some disease of the bone.

Hugh Owen Thomas[23] (1834–91) contributed to medical knowledge the fact that immobilization of a healthy joint does not lead to ankylosis. To disprove Paget's view, stated above, he quoted a case.

Two years ago I operated upon the feet of a lady suffering from contraction of the Achilles tendons, caused by the weight of the bed clothes during a long confinement to bed. The contraction had existed five years and totally prevented her locomotion, and she was consequently confined to a couch or bed during the whole of that period. Ten days after the operation she walked from my hospital, a distance of 800 yards, yet this joint had been fixed for a period of 5 years; there was not the slightest stiffness or adhesion in it. The stiffness was confined to the Achilles tendons only.

He also quoted a case described by Professor Flower :—

A man whose skeleton is at Marburg was encased by his relatives for twenty years in a space in which he could only sit with his limbs doubled up, and in which he could have had only very narrowly restrained movements of his joints; yet his limbs did not become deformed, and his joints retained their normal textures.

Thomas applied his knee splint to fractures of the lower limb.[24, 25] For the first month or so after the accident, the limb was treated by fixed traction in a bed knee-splint. Then the lower ends of the side irons were bent in to fit into a socket cut through the heel of the patient's boot, thus making what we now know as a walking caliper. While the patient walked in this his fracture consolidated. Referring to delayed union he wrote :—

Compressive fixation by the surgeon, having retained during treatment the part imperfectly supplied with blood . . . hindered the formation of a genuine repair. . . . In my opinion to apply an accurately fitted fixed dressing, such as for instance, a plaster-of-Paris bandage, is only to further delay the union and leave the restoration to chance.

However, as Thomas's hip splint gave way to plaster-of-Paris in the fixation of tuberculous hips, so has Thomas's knee-splint given way to walking plasters in the treatment of many fractures of the leg.

Krause[26] used a walking caliper for fractures of the femur, but in 1887 was apparently the first to use walking plasters for fractures of the leg. His method was as follows : Any deformity is reduced, and time then allowed for swelling to subside, compression and massage being employed if necessary. During this time the limb rests on a splint reaching above the knee, and fixing the ankle at right angles, or skin traction is used if there be any tendency to displacement. At the end of a week or so the skin is covered by two layers of muslin and an accurately moulded plaster cast applied, traction being maintained the while if there is any tendency to displacement. The knee is fixed in slight flexion, the ankle at right angles. The plaster extends from the heads of the metatarsals to mid-thigh. For malleolar fractures the plaster reaches only to just below the knee; for fractures

of the femur up to the tuber ischii. After the plaster has been applied, the patient remains in bed a further two days while it dries and then walks on the plaster unless the toes show much swelling. For walking in the street he is given a special laced boot that will fit over the plaster. During the early days of walking the toes become œdematous, but if use of the limb is continued this œdema (which spontaneously subsides during the night's rest) re-appears in smaller and smaller degree and finally disappears. Krause[27] writes of 98 fractures of the lower limb he had treated in walking plasters and found the time of healing much shortened by the method.

In 1894 Bardeleben[28] described his practice. He aimed at applying the plaster before any considerable swelling had arisen and said that in this way swelling was largely prevented. But if swelling should already have occurred this should not delay the application of plaster although a fresh plaster would be required when subsidence of swelling caused loosening. The plaster must also be changed if it is causing any localized pressure.

Korsch[29] applied plaster directly to the naked skin, which is thus better fitted and gripped. The skin was, however, previously greased to prevent actual adherence of plaster. He also used a metal stirrup for transmitting the patient's weight to the ground.[30] This was a U-shaped piece of iron, put to the ground in walking, whose side limbs were incorporated in the plaster and so indirectly gripped the tibial condyles. For fractures of the femur he incorporated part of the ring of a Thomas's knee-splint in the top of the plaster to give counter-traction against the ischial tuberosity. Another of Bardeleben's assistants, Albers,[31] made plaster do the work of this ring. He points out that when a walking plaster is removed the patient is able at once to walk without it. Any stiffness of the joints disappears in a few days.

In 1903 Guitard[32, 33] wrote on the ambulatory treatment of fractures of the lower limb, describing in particular the apparatus of M. Robert Sorel, his chief at L'Hôpital Pasteur du Havre. He refers to the stiffness that had come to be thought inseparable from treatment in plaster and attributes it to muscular atrophy, shortening of ligaments and capsule, and diminution of the area of articular cartilage. Traumatic effusions in ligaments, muscles, and cellular tissue may lead to fibrosis if the limb is kept motionless. Massage can get rid of these effusions and diminish pain, swelling, and wasting. But in the lower limb an even better method is available. By walking in his plaster the patient is spared the inconvenience of having to stay in bed—boredom, discomfort, general muscular weakness, loss of appetite, bronchopneumonia, expense—while bony union occurs more quickly than by any other method except massage and movement, which takes about the same time. Within the apparatus muscles contract, stiffness is prevented, and a good circulation maintained.

Many objections to the method had been raised. That there was not sufficient immobilization of the fragments, so that deformity would recur. That it was impossible to get a proper bearing for taking the patient's weight. That if padding separated the plaster from the skin it would become displaced and lumpy, whereas if there were no padding there would be pressure sores. Guitard observed that in practice deformity does not recur, while a slight degree of movement (as had been shown by Lucas-Championnière) helps union. The method is applicable to fractures and osteotomies of the leg or thigh, and to excision of the knee. The apparatus is applied as follows : Any deformity is reduced while traction and counter-traction

are exerted by the hands of assistants. A plaster-of-Paris bandage is then wound direct on to the skin, being well moulded to prominences and depressions and being thus enabled to fix the traction. A metal U similar to that of Korsch is then held in the axis of the limb so as to project 4 cm. below the heel, and is attached over the plaster by further plaster bandages. The patient can walk on the lower end of the U from the day following the application of the apparatus. For fractures near the ankle with displacement, the plaster must include the ankle-joint. For those at a higher level it stops below the malleoli. Above it finishes for fractured leg at the tibial tuberosities, for fractured thigh at the tuber ischii, these points bearing the patient's weight in walking. Fixation of joints is avoided when possible, as frequent movement of them was thought important to prevent stiffness. A photograph shows the foot bandaged to " avoid the œdema that is seen during the first days following the application " of the apparatus.

Korsch and Guitard did not immobilize the ankle-joint unless they thought this essential to the maintenance of the corrected position of the fracture in question. Delbet[34] introduced a skeleton below-knee plaster, consisting of a strip down each side joined by a band around the malleoli and a second band round the tibial tuberosities. The sole of the patient's foot was actually in contact with the ground as he stood, for the side strips stopped below the malleoli just short of the ground. Delbet claimed that weight would be transmitted from the upper part of the leg through the apparatus to the lower, but in practice the plaster merely splinted the malleoli from lateral displacement, and his photographs show that almost all his patients used crutches. For severe fractures such as Pott's fracture-dislocation the apparatus proved inadequate and window-œdema appeared between the strips, while for less severe fractures it was unnecessary. The fact that immobilizing an ankle-joint does not make it stiff invalidates the one possible object of the Delbet plaster.

During the war of 1914–18 Lorenz Böhler[35] adopted on a large scale plaster-of-Paris for treating the war fractures that came under his care in Austria. He had one great advantage over the previous advocates of plaster. Radiography had been introduced and perfected since the days of Krause, Bardeleben, and Sorel. That his methods closely resemble theirs can be appreciated by comparing their writings with his book and with the work to be seen in the Unfallkrankenhaus at Vienna.[36, 37] Great stress is laid on 'functional treatment', the patient using to an extent that must be seen to be believed the fractured part enclosed in plaster. Such natural use of muscles renders superfluous that poor substitute, massage.

Ability to walk within such a short time of sustaining a fracture is accounted for by the fact that the plaster transfers the patient's weight from some point above the fracture to the ground. In considering what this point is it is useful to remember how an artificial limb bears the patient's weight. The principle of tuber-bearing we owe to a mechanician named Bigg,[38] who wrote in 1855 :—

If after amputation above knee a stump thinly covered by integument remained, and a mere bucket or hollow wooden sheath were adjusted, regardless of anything but conformity to external shape, the effect would be to draw the flesh upwards and produce, not only painful, but injurious pressure on the end of the stump. Whereas, were that portion of the stump called the tuberosity of the ischium selected for the principal point of resistance, and the remaining part of the bucket left free, the patient would with ease rest the whole weight of his body upon the false leg without in the slightest degree uplifting the fleshy part of the stump.

The plaster applied for fractures of the upper end of the tibia encloses the whole thigh, so that the patient really sits on the top of it. This seat resembles the cup of a Hessing splint more than the ring of a Thomas's caliper. Pressure is also transmitted to the tibial tuberosities and tubercle, to the head of the fibula, and to the patella. These take all the weight in fractures of the lower end of the tibia, when the plaster is not carried up as far as the tuber ischii. The plaster even fixes traction by taking a grip of these points above and of the malleoli and foot below. The bony points are covered by aponeurosis, fascia, and little fat, and therefore the grip does not become loosened. The plaster is not removed until union is firm. After its removal swelling of the limb is prevented by bandaging. Joints show little stiffness, and this is soon remedied by use. As walking in plaster will induce a case of delayed union to unite, so does it assist the union of recent fractures. The impression of the accident on the patient's mind is minimized when he is able to walk about and live at home.

Since the publication in 1929 of Böhler's book describing his methods, the use of functional plasters has been widely adopted. It is found that a fracture causes least harm and inconvenience when during healing a plaster exo-skeleton does vicarious duty for a damaged endo-skeleton.

SUMMARY

In this history three phases in the use of plaster may be recognized. In the first all attention was concentrated on the bone, as is shown in the writings of Cheselden and Larrey. In the second, following Seutin and Lucas-Championnière, prior consideration was given to the soft parts. Krause and Böhler are outstanding names in the third phase, wherein fixation is so efficient that the limb may be used and kept supple without endangering the position of the bony fragments.

For more than 4000 years before Seutin there was little variation in the method of use of the starch or gum splintage. Occasionally someone would substitute plaster for gum, but the resulting splint was better than a strip of wood still only in its better fit. The apparatus was immovable and remained on the limb until union of the fracture was expected to be firm. It was generally extremely clumsy —for example, Larrey's conglomeration of bandages, leather, straw, string, and cushions of chaff, the whole saturated with white of egg and other substances. When the apparatus was removed the limb was found to be wasted and stiff. The principles of traction and counter-traction, however, were well understood.

Seutin first pointed out that rest in bed, though an excellent basis for the treatment of most illnesses, is actually harmful to patients recovering from fractures. The light, portable, starch apparatus that he introduced enabled his patients to make use of this knowledge, and, if the lower limb were fractured, they went about on crutches. Seutin's interest in the soft parts of the limb was shown by the way in which he split his apparatus to see that a satisfactory fit was maintained, and to make applications to the limb. These came to take the form of massage, later emphasized by Lucas-Championnière, and to this day massage of a limb that is supported by split plasters forms one method of treatment. To prevent stiffness, joints were moved as much as possible.

Mathysen's plaster bandages made the application of plaster-of-Paris comparatively simple, and for orthopædic purposes permanently replaced starch and

other hardening dressings. Thomas first made the patients walk in apparatus. thus bearing weight on the tuber ischii instead of on the axilla. They were enabled to continue exercising the limb while the bone united. Krause put plaster to the same purpose, while to Böhler is due the recent perfection of this technique.

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HÆMORRHAGE PER RECTUM AS AN INDICATION OF DISEASE IN A MECKEL'S DIVERTICULUM

By JUDSON T. CHESTERMAN

SURGICAL REGISTRAR, THE SHEFFIELD ROYAL HOSPITAL

THIS paper owes its inception to the fact that during the past three years there have been four cases of severe hæmorrhage per rectum owing to disease of Meckel's diverticulum in the surgical practice of the Sheffield Royal Hospital, and also it appears to be a condition of sufficient rarity and importance to warrant record.

The existence of the diverticulum was first noticed by Ruysch in 1701, but it was not until 1812 that the Tyrolese anatomist by whose name it is known pointed out its true embryological significance.

DISEASES OF THE DIVERTICULUM

The following general facts are of interest before considering one of its diseases in detail. In the 2 per cent of bodies containing Meckel's diverticulum, some $82\frac{1}{2}$ per cent of the diverticula are free-lying, 10 per cent have a free or attached band at the apex, 6 per cent show fistula, and the remaining $1\frac{1}{2}$ per cent show some other abnormality. In pathological conditions about five times as many males are affected as females, and this is greater than the proportional difference of the occurrence of the abnormality in the two sexes. Also at least 30 per cent of the lesions occur under the age of three years, and they are associated with other congenital abnormalities more often than any other form of 'acute abdomen' in childhood.

Owing to its origin, situation, and the aberrant mucosa it often contains, this diverticulum is subject to even more diseases than have brought an unenviable reputation to its near neighbour, the vermiform appendix. These may be classified as : (1) Inflammation—with or without ulceration ; (2) Obstruction—of itself or of the bowel by bands, intussusception, etc. ; (3) Fistula—congenital or acquired ; (4) Neoplasms—of which lipoma, myoma, myxoma, angioma, adenoma, carcinoma, sarcoma, and carcinoid tumours have been reported ; (5) Associated local abnormalities—mesenteric cyst, enterocystoma, and duplex ileum.

The literature on the subject is endless with the exception of this condition of bleeding per rectum, which has received but scant notice save in Germany and the United States. The first cases showing this type of hæmorrhage were reported in 1896 but were all due to intussusception of the diverticulum, and it was not until 1903 that Hilgenreimer placed on record a case of bleeding due to ulceration. Between 1903 and 1922 6 more cases were reported, but since then some 70 have been recorded, mostly from Germany and the United States. It is from a study of the Sheffield cases and of the available literature that the following facts have been gleaned.

ETIOLOGY OF THE HÆMORRHAGE

1. **Ulceration.**—The first cases to be recorded showed ulceration of the peptic type so frequently found in the stomach and the duodenum, and this resulted in a search for any factors in common. By serial section of thirty Meckel's diverticula Schaetz showed that 16 per cent contained aberrant gastric mucosa, and a further 5 per cent showed both aberrant gastric and pancreatic mucosa. This led to the supposition that the oxyntic cells of the aberrant mucosa secreted acid and so were the predisposing cause of the ulceration. The ulceration was found to occur in the aberrant mucosa, at its junction with the normal mucosa, and in the normal mucosa ; in fact, the majority seem to be situated in the latter position near the base of the diverticulum.

Operative and post-mortem records show that typhoid ulceration occurs in the diverticulum in association with the typical lesions in other parts of the bowel. Also tuberculous ulceration has been recorded, but as there was similar ulceration in the ascending colon, the hæmorrhage from the rectum could not be attributed to the condition of the diverticulum.

2. **Mechanical Theory.**—Quite apart from those operated upon for intussusception it was found that a certain number of cases showed ulceration when no aberrant mucosa was present. These were explained by Winkelbauer as being of traumatic origin. Irregular peristalsis produced either invagination of the apex or incipient intussusception of the base of the diverticulum into the small bowel, so causing either apical or basal ulceration.

3. **Recurrent Inflammation.**—A very few cases have been recorded of undoubted hæmorrhage from diverticula which showed no signs of either aberrant mucosa or of ulceration. All of these could not be accounted for by a mechanical theory, as the tip of the diverticulum was in some cases adherent to the mesentery or other loops of bowel, so preventing incipient intussusception or invagination with its resulting congestion and hæmorrhage. These, I think, must be due to recurrent inflammation of a hæmorrhagic nature or possibly to acute microscopic ulcers such as are alleged to occur in gastrostaxis.

4. **Infarction.**—Hunter records a case of melæna neonatorum which at autopsy proved to be due to infarction of the diverticulum, though I have been unable to find any other such case.

5. **Neoplasm.**—Finally, cases due to new growth of the diverticulum with the presenting sign of hæmorrhage per rectum have been recorded. Of the 9 I have been able to find, 7 were due to carcinoma or sarcoma, 1 to myoma, and 1 to adenoma of aberrant gastric mucosa.

DIAGNOSIS

In general it may be stated that 85 per cent of the cases are male, though two of the four new cases reported here are female ; that the age incidence varies from a few days to the sixth decade ; but that the average age at operation is a month or two over ten years.

The following, in their order of frequency, may be associated with the hæmorrhage from the rectum—anæmia, pain, vomiting, and bowel irregularity. The diagnosis is made by a process of exclusion, though hæmorrhage per rectum in a juvenile between the ages of 5 and 15, especially if a boy, is very suggestive.

The hæmorrhage is usually sudden and severe, though in cases of growth it may be slight and continuous. The blood is dark in colour, unless associated with diarrhœa, when it may be bright red, is thoroughly mixed with the stools, and unaccompanied by mucus. One case recorded by Stone showed umbilical hæmorrhage via a patent vitello-intestinal duct as well as melæna from an ulcer at the base of a diverticulum.

Pain occurs in about half the cases, is of colic type and never severe and prolonged unless associated with intestinal obstruction, and is situated in the umbilical region. The attacks of pain do not appear to have any definite relationship to food, as is so frequently found in peptic ulceration ; and no aggravating or relieving factors are mentioned in the case reports. In McKeen's case, a man aged 53, it preceded hæmorrhage by twenty years and only became severe at the onset of the bleeding which led to his admission to hospital.

In about a quarter of the cases nausea and vomiting occurred quite apart from any marked pain or obstruction. This is probably due to sudden local distension of a segment of the bowel giving rise to reflex sickness or as a reaction to sudden acute anæmia.

Bowel irregularity is rare, and was either diarrhœa following sudden severe bleeding into the lumen of the bowel, or rapidly increasing constipation which in every case necessitated urgent operation for acute intestinal obstruction.

If the blood loss has been acute, then the patient shows a typical hypochromatic anæmia but with increase of platelet count and of coagulation time, but when the loss is chronic, a colour index of 0·5 or lower is found.

In clinical examination the only positive finding is blood in the stools either as melæna or occult blood. Physical examination of the abdomen, sigmoidoscopy, and radiological examination, whether by barium meal or enema, are invariably negative.

In the child lesions of the alimentary tract such as gastro-enteritis, acute intussusception, and local ano-rectal conditions are easily excluded. Also the general diseases such as purpura, leukæmia, etc., should present no difficulty. In fact between the ages of 5 and 15 melæna is a very rare condition and should at once suggest the possibility of disease of Meckel's diverticulum.

In the adult the cause of the passage of bright red blood can usually be discovered by sigmoidoscopy and barium enema, though a single polypus or a localized area of hæmorrhagic colitis may cause difficulty when situated in the pelvic colon. But it should be noticed that these two conditions when associated with diarrhœa also show mucus in the stools, while red blood is always associated with diarrhœa and no mucus in diseases of the diverticulum. If there is left-sided enlargement of the heart, the blood-pressure should be taken, as hyperpietic patients occasionally suffer from bleeding due to rupture of a rectal blood-vessel. As the majority of cases show melæna rather than bright red blood, cirrhosis of the liver, peptic ulcer, and the less frequent cause, gastric carcinoma, must be excluded. The former is distinguished by hæmatemesis, ascites, splenic enlargement, and sometimes dilated veins on the abdominal wall, and the other two by history and X-rays. Of the rarer conditions causing melæna, primary peptic ulceration of the jejunum deserves notice. The very few cases recorded tend to show pain with a definite time relationship to food, periodicity, and attacks of melæna simulating a duodenal ulcer except that the pain is situated lower down and to the left of the umbilicus. In every case

X-rays showed obstruction, as the ulcer tends to encircle the bowel. However, as with peptic ulcer of Meckel's diverticulum, nearly all the cases were first seen after perforation or obstruction had taken place. Primary carcinoma of the small bowel gives rise to vague pain and attacks of colic in the left iliac fossa, sooner or later passing on to obstruction, melæna not being a presenting sign. One or two cases are reported of bleeding from diverticula other than Meckel's, and it is just possible that the diagnosis might be made by X-rays though impossible clinically. General diseases as a cause can be excluded by routine examination, blood' tests, etc.

TREATMENT AND PROGNOSIS

Treatment.—The treatment of the condition is surgical, and operation should be undertaken as soon as possible after diagnosis. Mason records five cases in which medical treatment was tried, after making the diagnosis of peptic ulcer of the diverticulum, and all ended fatally, surgery being invoked only after complications had arisen.

If the hæmoglobin is below 30 per cent, operation should be preceded by blood transfusion, which must be repeated rather than resort be made to the iron-deficient diet and prolonged rest usually prescribed by physicians for such conditions.

At operation resection of the diverticulum is all that is required.

Prognosis.—Greenwood states that for the ulcer group the mortality is 58 per cent of the perforated cases and 8 per cent of the non-perforated cases, and, as far as I can ascertain, the latter figure is accurate for all cases not showing perforation or obstruction at the time of operation.

CASE REPORTS

Case 1.—Male, aged 22, under the care of Professor Graham Simpson.

When aged 8 he suffered from lassitude for several weeks; this was followed by a sudden collapse on Boxing Day, 1921, when he passed a large quantity of bright blood per rectum. For some days after the stools were dark in colour, but there was no pain. He was seen by a consulting physician, but no diagnosis was made. He resumed normal life the following Whitsuntide, and there were no more symptoms until 1930, when he began to have attacks of discomfort in the abdomen and mild attacks of colic. He also had attacks of breathlessness and pain in the area supplied by the 3rd and 4th cervical nerves on the left side. The pain had no relation to food and there were no aggravating or relieving factors noticed. He was "off colour" the whole time until July 31, 1932, when without warning he was taken with severe hæmorrhage per rectum, the blood being of dark colour, unmixed with mucus, and the stools remaining discoloured for ten days.

On Aug. 3 he was admitted to hospital. Physical examination was negative, but there was much blood in the stools. Blood examination showed: Red blood-corpuscles 2,900,000, platelets 290,000, differential count normal, bleeding and coagulation times normal. The bleeding ceased after a blood transfusion given on Aug. 7. Plain X-ray of the chest and abdomen, barium meal, and barium enema were all negative.

On Sept. 8 he was discharged with the diagnosis of acute duodenal ulcer, and placed on medical treatment, which he has followed ever since.

On Jan. 11, 1933, he was re-admitted for hæmorrhage per rectum; this as in the last attack was unassociated with pain, and again complete radiological examination of the alimentary tract proved negative. He was discharged on Feb. 8, as both the patient and the consulting physician were against exploration. From February to the following Easter he suffered vague abdominal pain and was admitted again on April 5 with further hæmorrhage.

On April 10 Mr. J. C. Anderson operated for Professor Graham Simpson and found a large mass of tuberculous glands and adherent bowel in the ileocæcal angle; the loop was

resected, the two ends of the ileum were closed, and side-to-side anastomosis between the ileum and the cæcum was performed. On examination of the adherent bowel a Meckel's diverticulum was found containing a peptic ulcer $\frac{1}{3}$ in. in diameter. There has been no bleeding since, though he has suffered from vague indigestion for the past eight months. In December, 1934, physical examination and radiology showed no abnormality.

Case 2.—Female, aged 11, under the care of Mr. H. Blacow Yates.

This girl was staying in Derbyshire for the Easter week-end. On April 16, 1932, she was taken with sudden colic pain in the umbilical region followed by vomiting of food. This was immediately followed by the passage of a considerable quantity of blood, which covered her knickers and which her mother thought was her first menstrual period. The blood was said to be " fairly bright " but mixed with dark clots, and there was no slime on the knickers. The child went very faint, but this was attributed to the shock of seeing the blood; but two hours later a call to stool resulted in the further passage of blood. The motion next morning contained dark blood and she complained of feeling faint. That day (April 17) she was seen in consultation by Mr. H. Blacow Yates. Abdominal examination was negative except for slight tenderness just below the umbilicus. The rectum was entirely negative apart from containing dark blood. A tentative diagnosis of bleeding from a peptic ulcer of a Meckel's diverticulum was made and the child admitted to hospital. Previously the child had enjoyed good health and there had been no attacks of abdominal pain or dyspepsia.

Radiography of the alimentary tract was negative, as was sigmoidoscopy. Examination of the stools was negative, and the tourniquet test and platelet count seemed to rule out *purpura.*

On April 23 operation was performed after the case had been demonstrated as a case of bleeding ulcer from a Meckel's diverticulum to a post-graduate clinic. The terminal ileum was seen to contain dark bloody fluid, and a foot from the ileocæcal valve an indurated inflamed lump was found. This was seen to be a swollen congested Meckel's diverticulum adherent to the ileum above and to the adjacent mesentery. The diverticulum was easily separated from the gut and the mesentery. The distal half of the diverticulum was found

FIG. 193.—*Case* 2. External appearance of the diverticulum, showing the perforation of the viscus after separation from the mesentery.

FIG. 194.—*Case* 2. Internal appearance of the diverticulum, showing typical acute peptic ulceration.

to be acutely inflamed, œdematous, and indurated, whilst the peritoneal covering was acutely red. There was a minute perforation of the entire wall of the diverticulum after separation had been completed. The diverticulum arose from the antimesenteric border, was about 2 in. in length, and about $\frac{3}{4}$ in. in diameter at its junction with the ileum. It was resected with the endothermy needle and the opening sutured. The raw surface which had formed its bed on the upper surface of the mesentery was swabbed with spirit and peritonealized. There was no blood in the bowel above the origin of the diverticulum. The accompanying drawings illustrate the condition excellently (*Figs.* 193, 194). Section showed typical aberrant gastric mucosa around an acute peptic ulcer. No oxyntic cells could be demonstrated in the aberrant mucosa, however.

The child was discharged to the Convalescent Home on April 29, and in reply to a letter on May 1, 1935, her parents stated that she was in perfect health.

Case 3.—Female, aged 6, under the care of Professor G. Simpson.

On July 19, 1933, she was admitted with the following history: She had been admitted exactly a year before after a sudden hæmorrhage per rectum of bright red blood for about three days, followed by dark blood for about a week. Marked anæmia was present, but no other sign or symptom. Physical examination, including sigmoidoscopy, was negative and she was discharged. A year later a small hæmorrhage took place of dark blood and she was at once re-admitted. Physical examination and radiography were negative and a laparotomy was performed on July 27 with the pre-operative diagnosis of ? polyp ? ulcer of Meckel's diverticulum. Thirty-two inches from the cæcum a Meckel's diverticulum was found adherent to the right ovary. The diameter at the base was that of the small bowel, and it was about 2 in. long. It was resected.

She was discharged on Aug. 8, 1933, and it was stated that she had never had any trouble since, when seen in May, 1935.

PATHOLOGICAL REPORT.—Gastric mucosa present with peptic ulcer.

Case 4.—Male, aged 16, under the care of Mr. J. B. Ferguson Wilson.

The patient was admitted on Feb. 2, 1935, with the following history: In the later part of August, 1934, he was taken with slight colicky pain in the umbilical region lasting an hour or two, usually half an hour after food; this lasted a week. In October, 1934, he was pushing his bicycle up a hill when he was taken with diarrhœa and nausea. There was no pain and the stools contained dark blood without mucus and ceased in a few hours'
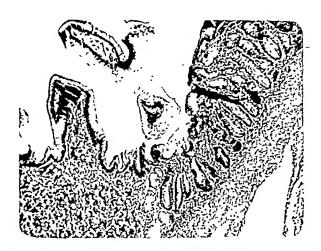
FIG. 195.—*Case* 4. Microphotograph showing aberrant gastric mucosa in a Meckel's diverticulum. (× 50.)

time. He went back to school in a fortnight's time, but suffered from spasms of colic in December and January, these nearly always occurring about an hour after breakfast, though occasionally at other times of the day. On Jan. 29 he was taken with severe colic for about ten minutes in the afternoon, and the next morning noticed bright red blood in the motions. On the evening of Jan. 30 he fainted while going to the w.c., was sick, and passed several very bloody stools. The next day he was seen by Mr. Ferguson Wilson, who diagnosed peptic ulcer of a Meckel's diverticulum and had him sent into hospital. Physical and blood examinations were negative.

On Feb. 9 he was operated upon, and a Meckel's diverticulum was found with the small intestine below it filled with blood but none above it. It was resected. On Feb. 23 he was discharged, and has had no further trouble since.

PATHOLOGICAL REPORT.—Sections show an acute peptic ulcer in the gastric mucosa of a Meckel's diverticulum (*Fig.* 195).

SUMMARY

1. Four cases of hæmorrhage per rectum due to peptic ulcer of Meckel's diverticulum are reported for the first time.

2. From the available literature the etiology of all forms of bleeding due to disease of this diverticulum is given together with the differential diagnosis.

3. Finally, laparotomy for the removal of an ulcer containing diverticulum is urged in children between the ages of 5 and 15 years showing hæmorrhage per rectum the cause of which is not revealed by sigmoidoscopy and blood examination.

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INTUSSUSCEPTION OF JEJUNUM INTO STOMACH THROUGH A GASTRO-ENTEROSTOMY STOMA

By J. A. MUNRO CAMERON

AND W. DOUGLAS MACFARLANE

VICTORIA INFIRMARY, GLASGOW

R. D., aged 52, dock labourer, was admitted to the Victoria Infirmary, Glasgow, first of all in April, 1928, when a posterior gastro-enterostomy was performed with invagination of a duodenal ulcer. He continued in good health, though suffering periodically from gastric discomfort, until January, 1934, when he complained of pain after meals, never of sufficient severity to make him stop work, and he was relieved in a short time by appropriate medical treatment.

FIG. 196.—Post-mortem appearance of intussusception of jejunum into stomach.

On July 9, 1934, he entered hospital free from any gastric symptoms, in order to have an inguinal hernia removed, and this was done on the following day under local anæsthesia. He was apparently quite comfortable until four days afterwards, when he complained of nausea and vomited some gastric contents. There was no pain. Vomiting then became bilious in character, later rather brown in appearance, and on the morning after he vomited 2 oz. of blood. Pain was now slight, but there was no rigidity or tenderness in any part of the abdomen except over his recent operation wound. No distension was evident, liver dullness was normal, and peristaltic sounds were heard on auscultation throughout the abdominal area. Later in the morning he again vomited small quantities of bright red blood and

seemed thereafter somewhat better; he was not distressed or restless, the pulse was 84 and of good volume. In the afternoon he became drowsy and soon began to sink rapidly; he died in the early evening just twenty-four hours from the onset of his first symptoms.

POST-MORTEM EXAMINATION.—A well-made, well-developed man; nothing of importance or relevance was found in the head or thorax; the operation wound was healing normally. On opening the enlarged and distended stomach, it was seen that a mass of congested and semi-gangrenous jejunum occupied the greater part of the cavity and was surrounded by dark effused blood (*Fig.* 196). On removing the organ, one was impressed by its most unusual weight.

Measurements.—The lesser curvature was 9 in. in length, the greater curvature 18 in., and the distance between these limits and over the anterior surface of the stomach was approximately 7 in. The intussusception measured $10\frac{1}{2}$ in. in length and the diameter of the stoma was about $1\frac{1}{2}$ in. Its condition was such that no reduction was possible without tearing the gut.

Histological Examination.—Sections of mucous membrane from areas around the stoma and from the jejunum were prepared. Intense venous congestion was apparent and a great deal of intercellular effusion, but putrefactive changes were so advanced that nothing further could be established. Even so, it was clear that during the twenty-four hours that the process had presumably taken, a very large quantity of fluid had exuded into the intussuscepted area.

COMMENTARY

Six years had elapsed from the original operation until death took place, an interval, curiously enough, which seems to be the recorded average. With the exception of Lewisohn's case (which occurred on the sixth post-operative day) a few months and five and a half years are the limits of time in which this complication has been observed after gastro-enterostomy, and the type of operation performed does not seem to affect the issue at all. Baumann reports one case of recurrence eight weeks after the initial reduction. This was relieved by resecting 10 cm. of intussuscepted jejunum.

The symptoms vary considerably in different patients. Pain is sometimes described as severe and cramping, again as just " tightness in the epigastrium ". In our case pain was never severe and for a long time was absent. Vomiting, first of gastric contents, then of bile, ultimately of blood in greater or less quantity, has always been described, and there is agreement in the rapidity with which patients go downhill.

Rigidity and distension are frequently marked, and in about 50 per cent there is a tumour-like appearance of the upper abdomen. The pulse is usually good until shock supervenes, and according to Shearer and Pickford this applies also to blood-pressure. They further state that there is no leucocytosis or rise of temperature.

Our report brings the total of published cases to 37, nearly all of which were first seen as surgical crises. But it is more than probable that an intussusception of this type is not so uncommon as that small number would suggest, and that a chronic or intermittent form may, in fact, follow many operations for gastro-enterostomy. Sibley has described an example of this kind. The patient complained of no pain or nausea or vomiting, but there was a feeling of constriction in the mid-epigastrium and inability to endure anything tight about the waist. The attack lasted for one to three hours after meals, and on fluoroscopic

examination it was found that a loop of jejunum had entered the stomach through a gastro-enterostomy stoma. At operation, though a large opening was present, no intussusception was found at that instant. The intussusception was present only after meals and presumably was effected during peristalsis, the large stoma accounting for the ease with which self-reduction was effected.

More than ten years ago Drummond suggested in this JOURNAL that the presence of the stoma may make possible a more rapid emptying of the stomach, with consequent irritation of the jejunal mucous membrane, sufficient at times to initiate antiperistalsis and lead to jejunal intussusception. More recent radiological knowledge has tended to confirm this view, and the demonstration of 'inflammatory cushions' round the stoma with concurrent jejunitis (Berg) has enabled us to visualize the mechanism by which antiperistalsis might be initiated.

In conclusion we would urge that the high mortality rate from this complication justifies us in drawing attention to it once more, and we feel, too, that only by systematic radiological examination after gastro-enterostomy can the incidence of the chronic form be revealed, a condition which might easily account for the otherwise inexplicable symptoms which sometimes follow gastro-enterostomy.

SUMMARY

1. An acute intussusception of jejunum into stomach through a gastro-enterostomy stoma is described as found at post-mortem examination.

2. A summary of the etiology and symptomatology of the recorded cases is given and the bibliography is brought up to date.

3. It is suggested that a chronic or intermittent form of intussusception, one example of which is epitomized, may be more common than is generally believed.

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A FURTHER NOTE ON THE DEVELOPMENT OF CYSTS IN CONNECTION WITH THE SEMILUNAR CARTILAGES OF THE KNEE-JOINT

BY ROBERT OLLERENSHAW

CLINICAL LECTURER IN ORTHOPÆDIC SURGERY, MANCHESTER UNIVERSITY

IN 1921 I reported in the BRITISH JOURNAL OF SURGERY[1] the first 3 cases of this condition to be recorded in English or American literature. In 1929, also in this journal,[2] I reported a further 18 cases and reviewed a number of reports by English and American surgeons, some of whom had dealt with as many as 11 cases. It was obvious that the condition was becoming well recognized. Since my last paper I have operated upon a further 20 cases, making 41 in all. In one patient the condition was bilateral, so that 42 knees were dealt with. As I said in my report of 1921, and as every observer has since agreed, the whole cartilage, with the cysts, must be removed to prevent recurrence. It is not clear from the published reports exactly how some of these writers have verified my statement that the whole cartilage must be removed; so far as I know, no clinical evidence has been produced by them. In my first paper I gave the history of one case in which the cyst only had been removed and which had developed a new and definite intra-cartilaginous cyst, causing symptoms, eighteen months later. It was on this case, and on the previously reported local excisions, with recurrence, of Ebner,[5] Riedel,[6] and Haehnel,[7] that I made the statement as to the total excision of the cartilage. I have had no opportunity since that time of further proof because in every case I have removed the whole cartilage. The fact that total removal of the cartilage is required is perhaps a point which helps to throw some light on the rather disputed etiology of the cysts.

If, as some are inclined to think, the cyst is purely degenerative and consequent upon a trauma to an area of cartilage, it would seem that the simple removal of the cystic portion should be sufficient to effect a cure and that, apart from further trauma, there should be no further development of cysts. But this is not the case; all who have reported personal experience of local removal are agreed that fresh cysts are formed without any evidence of further trauma and that complete excision of the cartilage is essential. One other point should be mentioned in connection with the traumatic degeneration theory. King[8] says that the usual history of trauma supports the view that the cysts are an acquired condition following upon injury and subsequent degeneration. Everyone will agree that the semilunar cartilage which is most commonly damaged is the internal, and it would therefore be natural to expect to find such degeneration cysts much more frequently in the internal than in the external cartilage. The opposite is the case; in the series which I now record, and which is the longest series so far published, the figures show only 6 internal cartilage cysts against 36 in the external cartilage. It is true that the cysts are generally found in the thicker, peripheral, portion of the cartilage, which is the

area most exposed to trauma, but in the new cases which I am now reporting I have found one case in which the cyst arose from the free border of the external cartilage and projected towards the middle of the joint, lying against the crucial ligaments.

This specimen is depicted in *Fig.* 197. It is the only case which I have encountered, or of which I have heard, in which the cyst projected to the centre of the joint and not towards the skin. It was removed from the joint of a girl aged 11 years who, at the age of 6, sprained the knee. Recovery appeared to follow, but after a few months (history is not quite definite on this point) the knee would 'go stiff' and the patient would limp. After a little exercise the stiffness and the swelling which always occurred would pass off. Limited extension of the joint had happened on several occasions. An exploratory arthrotomy was decided upon.

FIG. 197.—Cyst of the semilunar cartilage of the knee-joint.

OPERATION (Nov. 23, 1931).—General anæsthesia. The skin was incised along the long axis of the limb and the patella split longitudinally. On retraction a cystic swelling, the size of a cherry, was found to be attached to the free (medial) edge of the outer semilunar cartilage and lying closely against the crucial ligaments. The cartilage was an unusually broad one. It was excised completely with the cyst. In freeing the anterior attachment the cyst, which was very thin-walled in that region, was accidentally burst and the usual gelatinous contents escaped. The patella was approximated and the tendon sutured with catgut; no sutures were passed through the bone. The recovery was uninterrupted and the girl has had a normal joint in appearance and in function since that time.

There has been a considerable amount of discussion as to the nature of the cysts and their microscopical structure. All the sections of my specimens have been made by the same pathologist (Dr. C. E. Jenkins) and every cartilage removed has been examined by sections. We believe that an endothelial lining to the cysts can be demonstrated, and in my 1929 paper sections were shown which appeared to us to establish that point. Kleinberg,[2] reporting one case, found a flat layer of

endothelial cells lining the cyst, and suggested that these cells arose from lymph vessels. Zadek and Jaffe[4] refer to sections of their specimens removed at the New York Hospital for Joint Diseases, and find a definite layer of endothelium particularly lining the smaller spaces. Others have not been able to identify this layer. I have therefore asked Dr. Jenkins to append his views to the present report.

ANALYSIS OF PRESENT SERIES OF 20 ADDITIONAL CASES (21 KNEES)

Males	16
Females	4
Ages .. .. From 11 to 58 years	
External cartilage affected	19
Internal cartilage affected	2
Right knee affected	11
Left knee affected	10
Bilateral	1

ANALYSIS OF WHOLE SERIES OF 41 CASES (42 KNEES)

Males	33
Females	8
Ages .. .. From 6 to 58 years	
External cartilage affected	36
Internal cartilage affected	6
Right knee affected	20
Left knee affected	22
Bilateral	1

THE NATURE AND RECOGNITION OF ENDOTHELIUM : WITH SPECIAL REGARD TO THE SILVER METHODS OF STAINING

By C. E. JENKINS

We define 'endothelium' as any specialized layer of cells derived from the mesoderm and lining a cavity. In our view the term should not be restricted to the types of cells found in the circulatory system, but should include synovial cells also. It may well be that the cells lining the cartilage cysts have affinities with synovial cells ; on that point we offer no definite opinion. King[8] suggests that by the use of silver staining we may decide definitely that the lining cells are not vascular endothelium. The value of silver impregnation as a differential stain can be exaggerated. Silver stains intercellular material; consequently, tissue rich in this substance takes the impregnation extensively and in proportion to the intercellular material which is present. A cross-section of a blood-vessel so stained does not show the endothelial layer because the cement substance is in a plane too small to be visible. But to assert that vascular endothelium does not stain with silver is incorrect. The metal can, in fact, be used to demonstrate the differences in the endothelium of arteries, veins, and lymphatics.

No reliance can be placed upon silver as a means of demonstrating cells. The two photomicrographs which accompany this note illustrate this fact clearly. *Fig.* 198 is a section of an external cartilage cyst stained with silver alone. The cover-slip was then removed, the section counterstained with hæmatoxylin, and the same area photographed again. The greater number of cells shown in the second photomicrograph (*Fig.* 199) needs no comment. It will be seen, further, that there is a definite aggregation of cells close to, and on, the surface.
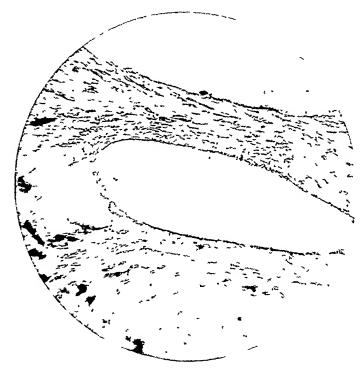
FIG. 198 —Sections of a cyst of the external cartilage stained with silver alone.
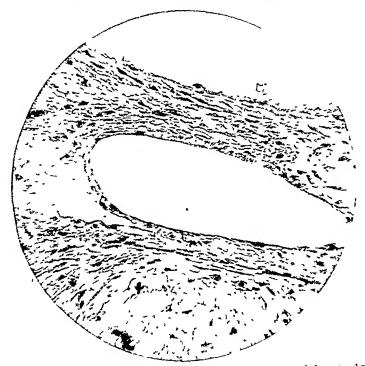
FIG. 199.—Section of area shown in *Fig* 198 after counterstaining with hæmatoxylin.

This, in our observations, is common in all the smaller cysts. Large cysts, admittedly, do not show the same appearance, possibly because they have reached full development and the unknown process which generated them has burnt itself out.

CONCLUSIONS

1. A further 20 cases of cysts in the semilunar cartilages of the knee-joint are reported—18 external and 2 internal.

2. Cartilage cysts may arise, as is now shown, from the free border of the semilunar cartilage and project into the joint, producing occasional ' locking ' symptoms, with the sensation of ' locking ' and followed by effusion into the joint.

3. Further experiences than those recorded in 1921 and 1929, and the use of other staining methods, still convince us that the smaller cysts can be shown to be lined by endothelium.

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ANGIOMA OF THE KIDNEY

REPORT OF A CASE WITH AN ANALYSIS OF 26 PREVIOUSLY REPORTED CASES

By R. H. JOCELYN SWAN

SURGEON EMERITUS TO THE CANCER HOSPITAL, LONDON

AND HAROLD BALME

BENIGN tumours of the kidney very rarely cause any clinical symptoms necessitating surgical interference, but villous papillomata of the renal pelvis and cavernous angiomata of the renal tissue may cause sudden and profuse hæmaturia which demands operation as an urgent life-saving measure. One of us (R.H.J.S.) reported a case of cavernous angioma of the kidney in 1921, since when other cases have been recorded, though in some the evidence is somewhat doubtful. A second case recently came under our care which is now reported, and an attempt will be made critically to review the cases previously recorded, and also to bring out a few points which may be of assistance in dealing with similar cases.

CASE REPORT

C. S. L., aged 15, a schoolboy at a well known Public School, commenced a fairly profuse hæmaturia on the morning of Nov. 2, 1934, unaccompanied by pain, frequency, vesical irritability, or pyrexia. Apart from some chest affection in childhood he had always been a strong and healthy lad, and there had been no previous attack of hæmaturia nor had there been any symptoms attributable to disease of the urinary tract. Three days prior to the onset of hæmaturia, he had sustained a kick in the scrotum whilst playing football, but recovered after a short interval and resumed the game and played a further game without discomfort two days later.

As soon as the hæmorrhage was reported, the boy was put to bed in the College Sanatorium and placed on a bland fluid diet. The temperature and pulse were normal; there was no swelling, no evidence of trauma nor tenderness in either renal angle. Neither kidney could be palpated. The subsequent history of the case and the investigations carried out are best given in chronological order.

Nov. 4.—Temperature and pulse normal, but hæmaturia persisted. The urine was heavily loaded with red blood-cells with a normal complement of leucocytes. No casts or pus were present, but a number of acid-fast and alcohol-fast bacilli were found in the centrifuged deposit, suggestive of tubercle bacilli. The specimen was not drawn by catheter, but a guinea-pig was inoculated from the deposit.

Nov. 7.—Hæmaturia still present but in diminished quantity. No rise in temperature or of pulse-rate, and no discomfort nor frequency in micturition. A catheter specimen of urine was examined, but no organisms were present and no pus cells found.

Nov. 10.—Hæmaturia now ceased and urine was bright and clear. Slides of the organisms reported on Nov. 4 were submitted to another bacteriologist, who was of opinion that they were not tubercle bacilli but a non-pathogenic streptothrix.

Nov. 14.—Blood examination showed :—

Red cells	..	.. 6,000,000	Polynuclear basophils ..	1%
Hæmoglobin ..	..	.. 98%	Polynuclear eosinophils ..	6%
Colour index..	..	.. 0·8	Lymphocytes ..	.. 48%
Platelets	..	540,000	Monocytes	.. 9%
Coagulation time	..	7 minutes	Red cells normal in shape, size, and	
White cells ..	..	.. 8400	staining reactions	
Polynuclear neutrophils	.. 36%			

Nov. 18.—Further catheter specimens examined and no organisms found.

Nov. 20.—Patient allowed out of bed; hæmaturia recommenced without any other urinary symptom. Transferred to Edenbridge District Hospital.

Nov. 23.—Hæmaturia persisting. Cystoscopic examination. Bladder and ureteric orifices were normal. Blood in forcible efflux from left orifice; clear urine from right. Intravenous indigo-carmine appeared from each side in six minutes, rapidly increasing to a deep blue on right side and a black coloration on left side, due to admixture with blood. Transferred to London for further investigation.

Nov. 27.—X-ray examination. No evidence of renal calculus. A calcified tuberculous mesenteric gland gave a rounded, mottled shadow on the left side of the fourth lumbar vertebra.

FIG. 200 —Pyelogram obtained ten minutes after intravenous injection of uroselectan B. The upper calix of the left kidney is narrowed and mottled in appearance.

Intravenous pyelogram with uroselectan B (*Fig. 200*). Right shadow showed normal pelvis and calices. Left kidney—small bifid pelvis with clear lower calices, but the upper calix was elongated and ill-defined, with an area of irregular, mottled appearance suggesting tuberculous infection.

Urine: acid; specific gravity 1020; albumin in small quantity; blood discs present and numerous oxalate crystals. No pus cells, casts, tubercle or other organisms found. Blood :—

Red cells	..	4,720,000	Leucocytes	.. ..	7000
Hæmoglobin	..	85%	Polymorphonuclear cells		61·7%
Colour index	..	0·9	Lymphocytes	.. ..	33%

Nov. 28.—A low spinal anæsthetic was given in order to carry out an ascending pyelographic examination, but it was found impossible to pass ureteric catheters into either ureter for more than 2 cm.

Nov. 29.—X-ray examination of chest by Dr. Coldwell showed no evidence of tuberculous disease either in lungs or in the mediastinal glands. There was a small adhesion between the base of the left lung and the diaphragm.

Nov. 30.—The patient was awakened in the early morning by a severe pain in the left loin passing forward around the iliac crest to the groin, and followed later by marked hæmaturia with some clots. Consultation with Dr. Scott Pinchin, who could find no sign of active tuberculous disease in the chest. A culture from a throat swab showed no hæmolytic streptococci, but a Mantoux intradermal test was positive. The urine contained a quantity of blood, but no increase of leucocytes, and tubercle bacilli could not be found.

Dec. 6.—Bleeding continued in the urine in varying amounts—sometimes profuse, sometimes only slight. The boy was becoming decidedly anæmic, and, as it seemed that the
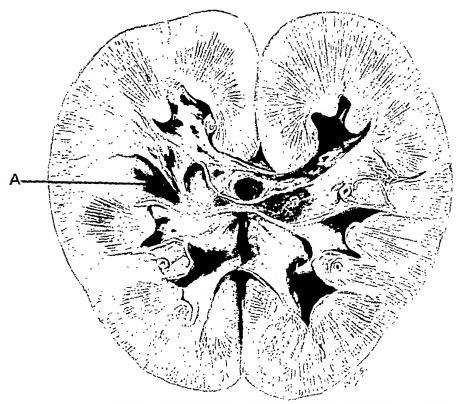
FIG. 201.—The kidney bisected after removal. The angioma is seen at A and there is considerable staining of the pelvis and subepithelial tissues from hæmorrhage.

diagnosis must rest between tuberculous disease and a hæmorrhagic tumour of the left kidney, operation was advised, and the patient was again transferred to Edenbridge District Hospital.

OPERATION (Dec. 12).—Evipan and gas and oxygen anæsthetic by Dr. Jarman. The kidney was rapidly exposed by an oblique lumbar incision, easily separated, and brought to the surface. It appeared to be quite normal. The ureter was not thickened and the pelvis appeared to be normal, although discoloured by contained blood. The upper pole of the kidney contained a small thickened area about the size of a large pea, which was thought to be a tuberculous focus; the kidney, together with the proximal 6 in. of the ureter, was therefore removed, and the wound closed with a small posterior drain.

Convalescence was uninterrupted and the patient made an excellent recovery.

PATHOLOGICAL REPORT.—For the following pathological report we are indebted to Dr. Hawksley :—

A kidney of normal size and contour. From urine (blood-stained) obtained from it before it was incised, films were made; another part was inoculated into a guinea-pig. The films were negative for tubercle bacilli and other organisms, and the guinea-pig, killed in the fifth week, showed no evidence of tuberculosis.

After fixation the kidney was bisected longitudinally (*Fig.* 201). The pelvis was bifid; the parenchyma was of healthy appearance. Pelvis and calices throughout were mottled with blood. In one of the upper calices, at one side of a pyramid, was a soft red mass of tissue, 10 by 4 mm. in diameter. Two pieces from this area and two from other parts were taken for section.

Microscopically (*Fig.* 202), there is no abnormality in the latter beyond a little sub-epithelial hæmorrhage. In the former there is evidence of the existence of a capillary angioma the tenuous walls of which have ruptured; the histological picture is complicated by extensive effusion of blood into the subepithelial tissue, largely masking the structure of the remaining intact capillary network. A feature of interest is the apparently intimate relation of the angiomatous tissue to vasa vasorum of arterioles in the connective tissue.
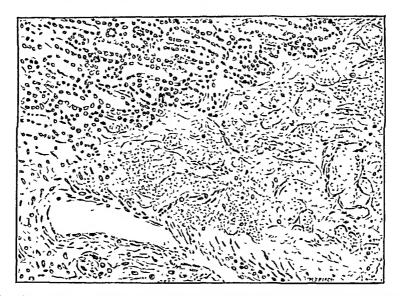
Fig. 202.—Microscopical section of the angioma and adjacent renal tissues at the point marked A in *Fig.* 201.

The neighbouring renal substance is of normal structure and entirely free from interstitial hæmorrhage.

A study of the various sections suggests that an abnormal proliferation of capillary blood-vessels, probably of developmental origin, has taken place immediately beneath the epithelium of the calix; rupture of these vessels has resulted in extravasation of blood into the pelvis and the subepithelial tissue.

DISCUSSION

In the consideration of this case we were presented with a patient of 15 years of age who had sudden profuse unilateral renal hæmaturia lasting for eight days and recurring after only slight exertion. The early report of the presence of acid-fast bacilli in the urine raised the suspicion of tuberculous disease in the kidney, whilst the subsequent findings on clinical examination of an old tuberculous cal-careous gland, of an old adhesion between the pleura and the diaphragm, of a

positive Mantoux intradermal test, and of the mottled appearance of the upper calix of the kidney in an intravenous pyelogram were all points which lent support to this view. On the other hand, however, the complete absence of pus in the urine, the inability to find at any time after the first examination any bacilli in the urine, and the absence of any increased frequency of micturition, were points against the diagnosis of renal tuberculosis. The rapid excretion of indigo-carmine from the bleeding side of intense coloration was also unlike a tuberculous infection. The organisms first reported were also subject to suspicion as the urine containing them was not catheter-drawn, and was passed into a vessel which could not be guaranteed free from contamination, whilst the organisms themselves, though alcohol-fast (and therefore not smegma bacilli), were considered by one bacteriologist to be merely a non-pathogenic streptothrix. The fact that an organism so similar to the tubercle bacillus may be found under circumstances which would suggest a urinary infection is worthy of note.

We had therefore to consider other causes of unilateral renal hæmaturia. Hæmorrhage of purpuric origin was excluded by the blood-picture. Calculus in the kidney was unlikely, in the complete absence of any shadow taken in several X-ray films, whilst hæmorrhage from a toxic nephritis was negatived from the fact that both during and after the hæmaturia, bacteriological examinations of catheter specimens of the urine were sterile and that, in the absence of blood, no albumin or casts could be found ; nor could any evidence of a focus of septic infection be discovered. That the blood came from the left kidney could not be doubted, as a blood-stained efflux was seen from the left ureter on more than one occasion in a full and forcible flow. The mucous membrane of the bladder was everywhere normal and showed no areas of submucous hæmorrhage nor any sign of papillomatous growth. The diagnosis seemed therefore to rest between an early tuberculous infection of the kidney and some form of neoplastic growth. Hypernephroma or carcinoma was unlikely, owing to the youth of the patient, whilst sarcoma or an embryonic tumour usually occurs in infants and gives rise to an easily palpable renal tumour. We could not exclude a villous papilloma of the renal pelvis in the pyelogram, but these cases are very rare and usually in older patients. The fact that the pyelogram showed a bifid pelvis suggested some congenital abnormality which might account for the hæmorrhage. In this connection it is worthy of note that in the cases of renal angiomata recorded by Kidd,[5] Bailey,[15] and Gayet, Gabrielle, and Martin,[18] it is definitely stated that a double or bifid pelvis was found.

The pyelogram in our case showed a small mottled area with ill-defined margin in the upper calix. A similar appearance has been noted in other cases by Jenkins and Drennan,[10] and by Gayet, Gabrielle, and Martin.[18]

We may be criticized for carrying out an operation without awaiting the result of the inoculation of the urinary deposit into a guinea-pig (which, as a matter of fact, subsequently proved negative), but the continuance of the hæmorrhage and the progressive anæmia of the patient rendered it advisable, though not an immediate necessity as in our earlier case. In any event, had the inoculation proved positive, nephrectomy would have been necessary, whilst if negative, the possibility of some form of growth would have rendered exploration and probably nephrectomy advisable. The other kidney having been proved functionally active, operation was therefore advised without further delay, after full and frank discussion with the patient's father.

The full pathological examination of the kidney after removal by Dr. Hawksley, Senior Pathologist to the Cancer Hospital, showed the presence of a capillary angioma with thin walls of flattened endothelial cells, which had ruptured, causing extensive blood effusion into the subepithelial tissues and into the renal pelvis. The tumour was situated at the side of the base of an upper pyramid, and is therefore distinct from the cases described by Fenwick,[19] Newman,[20] Simpson,[25] and others in which bleeding occurred from an angioma situated at the apex of a papilla.

REVIEW OF THE LITERATURE ON RENAL ANGIOMATA

There is very brief mention by pathologists of the occurrence of angioma in the kidney, but Stieda[24] states that Fukuda found two cases of angiomata of the renal parenchyma in the course of post-mortem examinations. The case described by Morris[1] was found in the kidney of a young woman who died from septicæmia, but who was known to have had occasional attacks of hæmaturia, lasting for three to four days, and pain in the left side for some years. In this case multiple angiomata were present, one of which had ruptured into the upper calix. Kaufmann[31] says they are very rare, and Kidd stated in the discussion following the exhibition of my first case before the Urological Seation of the Royal Society of Medicine,[2] that in a series of 2500 post-mortem examinations which he had personally conducted and in which he had particularly searched for renal angiomata, he had failed to find one ; he had found adenomata and fibromata, but these had not given rise to clinical symptoms. Mackey[16] states that Muir had found no specimen of renal angioma at post-mortem examinations in Glasgow.

A careful search of the literature shows that 25 cases have been recorded, to which we now add another, and by the kindness of Mr. J. C. Anderson, of Sheffield, we are able to include a further case as yet unpublished, in this manner making a total of 27 cases (*Table I*). Of this number, 19 showed an angiomatous tumour in the kidney, occurring most frequently in the subepithelial tissue around the base of a pyramid, whilst in 8 cases the angioma was present at the apex of a papilla.

SYMPTOMATOLOGY

In the first case, which was operated upon in 1906 and described in 1921,[2] the hæmorrhage was very profuse in the first onset, and similar profuse bleeding from the onset is quoted by Wheeler,[8] Jenkins and Drennan,[10] and Mackey,[16] demanding immediate operation, whilst in others quoted by Kidd,[5] Lutz,[6] Suter,[7] Gayet, Gabrielle, and Martin,[18] and Everidge,[14] there had been intermittent attacks of hæmaturia culminating in a more serious bleeding demanding operation.

It is interesting to note that in these cases of intermittent hæmorrhage, the attacks of bleeding had in some cases extended over many years, often after long intervals during which the patient appeared to be perfectly well. In Judd and Simon's case[11] the patient had had attacks of hæmaturia at intervals of four to five years for twenty years, being at times very severe, whilst in the careful report by Gayet, Gabrielle, and Martin[18] unilateral renal hæmaturia had been present for ten years, with intervals between the attacks of five and three years respectively, but becoming increasingly frequent. In Jenkins and Drennan's case[10] a patient aged 32 years had had attacks of hæmaturia at the age of 25 and 27 years, but was

Table 1.—Renal Angiomata

No.	Author	Age and Sex	Side	Symptoms	Operation	Situation of Lesion
1	Morris (1901)	23 F.	L.	Intermittent profuse hæmaturia and left lumbar pain for some years	—	Multiple angiomata one of which had opened into upper calix. Post-mortem specimen
2	Swan (1921)	19 M.	L.	Sudden very profuse hæmaturia for 3 days	Nephrectomy ..	Cavernous angioma of central portion of medulla and renal pelvis
3	Deansley. Reported to Swan (1921)	66 M.	L.	Intermittent hæmaturia and pain in left loin for 5 months	Local excision ..	Rounded angiomata on surface ⅛ to ⅓ in. in diameter. One excised. Hæmaturia and pain persisted
4	Sennels (1922)	35 M.	L.	Hæmaturia and pain for one week	Nephrectomy ..	Angioma size of a pea in wall of pelvis
5	Kidd (1924)	19 M.	R.	Attacks of bleeding and colic for 10 years. Finally urgent	Nephrectomy ..	Subepithelial angioma of upper calix with hæmorrhage into renal tissue. Double ureter
6	Lutz (1924)	62 M.	R.	Hæmaturia for 5 weeks ..	Nephrectomy ..	Angioma size of cherry stone at junction of medulla and pelvis and under epithelium of calix
7	Suter (quoted by Lutz) (1924)	32 F.	—	Frequent hæmaturia for 1¼ years, increasing in amount	Nephrectomy ..	Angiomata in wall of renal pelvis
8	Wheeler (1924)	37 M.	L.	Very profuse hæmaturia 6 days. No pain	Nephrectomy ..	Angioma 1¼ cm. in diameter in wall of pelvis with extravasation of blood into renal tissue
9	Begg (1926)	33 M.	R.	Hæmaturia after a strain 2 years previously. Second attack nearly continuous for 6 months, becoming urgent	Nephrectomy ..	Lower pole of kidney occupied by a large blood cyst 11 cm. in diameter which was considered to be due to hæmorrhage from an angioma. Cavernous tissue found present in wall of cyst
10	Jenkins and Drennan (1928)	33 F.	L.	Attacks of hæmaturia at intervals of 2 and 6 years. Last profuse with colic	Nephrectomy ..	Angioma in upper pole 1 in. in diameter bulging into upper calix
11	Judd and Simon (1928)	57 F.	L.	Attacks of hæmaturia at intervals of 4 to 5 years for 20 years, sometimes profuse with colic	Nephrectomy ..	Angioma in upper pole of kidney 2½ by 1½ cm.
12	MacKenzie and Parkins (1929)	35 M.	L.	Hæmaturia for 10 days ..	Nephrectomy ..	Angioma surrounding and opening into upper renal calix with hæmorrhage into tissue

14	Everidge (1930)	19 M.	L.	Intermittent haematuria for some years	Nephrectomy	..	pelvis. Cavernous angioma Subepithelial angioma of pelvis
15	Bailey (1930)	31 F.	R.	Intermittent profuse haematuria for 2 years; 2 to 3 months intervals	Nephrotomy and decapsulation. Nephrectomy 2 years later	2	Angioma size of pea lying between two upper pyramids. Only found after multiple sections of kidney
16	Mackey (1930)	61 F.	R.	Profuse haematuria and colic for 8 days. Urgent	Nephrectomy	..	Small angioma of lower mid calix with surrounding hæmorrhage
17	MacKenzie and Hawthorne (1931)	30 M.	L.	Haematuria 8 years before. Recurred and persisted for 10 days, with colic	Nephrectomy	..	Angioma of pelvic wall
18	Gayet, Gabrielle, and Martin (1934)	33 M.	R.	Attacks of haematuria and colic for 10 years. Later profuse	Nephrectomy	..	Angioma 2 cm. in diameter in medulla and submucous tissue of upper calix
19	Swan and Balme (1935)	15 M.	L.	Haematuria for 8 days recurring after interval of 10 days	Nephrectomy	..	Subepithelial angioma of upper calix

Angiomata of Apex of Pyramid.—

20	Fenwick (1903)	40 F.	R.	Continuous haematuria 2 years. No pain	1. Nephrotomy. 2. Nephrectomy 2 months later	..	Angioma of capillary type (Targett) of lower papilla
21	Newman (1913)	54 M.	L.	Frequent attacks of haematuria for 3 years, becoming profuse. No pain	Nephrectomy	2	Angioma like a mulberry mass in upper pyramid. Distinct limiting membrane
22	Baum (1913)	22 M.	L.	Intermittent haematuria for 10 years. Never pain	Nephrectomy	..	Angioma of apex of papilla
23	Rousing (1918)	—	—	Profuse haematuria ..	Nephrectomy	..	Angioma of papilla size of a pea
24	Burgess (1922)	26 F.	R.	Haematuria 4 days. No pain	Nephrotomy and excision of whole papilla	..	Capillary angioma. Remained well for four years
25	Stieda (1923)	29 M.	R.	Haematuria for 6½ years	1. Decapsulation. 2. Nephrectomy	..	Haemorrhage continued after decapsulation. Angioma of papilla
26	Simpson (1926)	30 F.	R.	Profuse haematuria for 4 days. No pain	Nephrectomy	..	Small cavernous angioma of tip of papilla
27	Anderson (as yet not published)	45 M.	R.	Haematuria of varying degree for 7 weeks	Nephrectomy	..	Angioma of apex of papilla in uppermost calix

then free from bleeding for six years, when again a profuse hæmorrhage occurred. In Kidd's case[5] there had been attacks of profuse hæmaturia for ten years, but in the attack for which the patient came under observation the hæmorrhage was so severe as to demand immediate operation. In MacKenzie and Hawthorne's case[17] there had been only two attacks of bleeding at an interval of eight years. In just half the cases recorded the hæmorrhage commenced as an acute bleeding for which operation had to be undertaken owing to the fact that no treatment was effectual in controlling it.

Lumbar pain is mentioned as being present in addition to the hæmaturia in 11 cases, usually as distinct colic and probably due to the passage of blood-clot down the ureter. In 2 cases it is described as an aching pain. It is perhaps significant that of the 8 cases in which an angioma was found present at the apex of a pyramid, it was definitely stated in 7 cases that no pain was present at any time, whilst in the remaining one no mention was made of its presence. In 2 of this group the hæmaturia was serious enough to demand rapid surgical interference (Simpson[25] and Burgess[23]), and it is possible that the immediate admixture of blood oozing from the apex of a pyramid with the urine contained in the renal pelvis prevented any clotting or obstruction to the normal passage along the ureter.

The consideration of the age of the patient at the first onset of hæmaturia may be of some assistance in arriving at a diagnosis in these cases, and it is a significant fact that in the recorded cases the primary bleeding occurred comparatively early in life. Thus in 26 cases in which the age is stated the first attack of hæmaturia commenced as follows :—

						Per cent
Between	1–10 years in	1	case	..	..	3·8
	11–20 ,,	5	,,	..	..	19·2
	21–30 ,,	8	,,	..	..	30·8
	31–40 ,,	7	,,	..	..	26·8
	41–50 ,,	1	,,	..	..	3·8
	51–60 ,,	1	,,	..	..	3·8
	61–70 ,,	3	,,	..	..	11·5

From the above table it will be seen that in 80 per cent of the recorded cases, the first appearance of blood in the urine occurred before the age of 40 years, whereas it is very unusual to find a hypernephroma or a carcinoma of the kidney before this age.

ANATOMICAL SITUATION OF ANGIOMATA IN THE KIDNEY

Although angiomata may occur in any part of the kidney, the majority of the lesions reported in the literature appear to be a cavernous or capillary angioma situated immediately beneath the mucous membrane lining the pelvis or one of the calices of the kidney, rupturing through the latter and giving rise to hæmorrhage. In many cases there is recent hæmorrhage into the immediately surrounding renal tissue, though in some reports mention is made of a limiting fibrous capsule. In 1 case a cortical angioma was resected from the kidney, but the hæmaturia persisted, and it is possible that in this case another deeper-seated tumour was present. In 4 cases a distinct angiomatous tumour was found on bisecting the kidney, after removal, but in each the tumour mass encroached upon the renal pelvis or a major

calix, and probably for this reason gave rise to hæmaturia. In 8 cases the angioma is reported to have occupied the tip of a pyramid of the kidney, giving rise to hæmorrhage severe enough to warrant nephrectomy in 7 cases, whilst in 1 case, reported in detail to me by Burgess,[23] the whole papilla, containing an angiomatous mass the size of a green pea, was resected and the patient remained free from any symptom for four years after operation.

Only in rare instances has a tumour been seen on the surface when the kidney was exposed at the operation, and most contributors state that the kidney appeared to be normal until it was bisected. In Deansley's case[3] there were several rounded nodules ½ to ¾ in. in diameter on the cortex of the kidney, one of which was removed and reported by Targett to be an angioma surrounded by a fibrous capsule. The kidney was not removed and hæmaturia continued. In the case described by Judd and Simon[11] in which occasional attacks of hæmaturia had been present for twenty years, a tumour measuring 2½ by 1½ cm. was present in the upper pole of the kidney, whilst in Gile's case[13] a lobulated tumour measuring 6 cm. in diameter was found at the anterior surface of the kidney, but extending into the pelvis. Begg[9] removed a kidney containing a large blood cyst 11 cm. in diameter which was considered to be due to hæmorrhage from a renal angioma, cavernous tissue being found present in the cyst wall. In the remaining cases no tumour could be felt from the outside on exposure of the kidney at operation, which was necessitated in most cases by the severity or the continuance of the hæmorrhage which had been localized to one kidney.

DIAGNOSIS

The diagnosis of a renal angioma is very difficult and in most cases is made after the kidney has been removed for urgent hæmaturia. Practically all the recorded cases were proved to have unilateral renal bleeding, shown by cystoscopic examination and confirmed on subsequent examinations, and it remains to consider the various causes of bleeding from one kidney.

Hæmorrhagic nephritis can be excluded by the absence of casts or of albumin in the absence of blood, and the failure to find a marked septic focus, whilst the cystoscopic proof that the bleeding is unilateral and the frequent occurrence of one-sided colic from the passage of clots down the ureter will help to exclude it.

Tuberculosis would naturally be suspected in a young patient with unilateral hæmaturia, but will usually be excluded if the findings in the urine are negative, although the absence of small quantities of pus and of tubercle bacilli might be regarded as due to temporary closure of the infected calix. Repeated examinations of the urine and the complete absence of pus and of bacilli, together with the freedom from dysuria and increased frequency of micturition and the absence of any change in the ureteric orifice on cystoscopic examination, would negative tuberculous disease. Inoculation of guinea-pigs with the deposit of a suspected urine might be valuable in some cases.

Renal calculus may occasionally cause unilateral hæmaturia, even without pain, but with the present improved technique of radiology, very few calculi will escape detection on a good X-ray film.

Renal growth must be especially considered, particularly in patients over 45 years of age, but we find that nearly 80 per cent of cases of angioma occur before that age. In no case could any enlargement of the kidney be detected on deep

palpation in the loin, and it is improbable that a normal pyelogram would be obtained in any case of renal tumour.

Pyelographic examination was carried out in 9 of the 27 collected cases and some points arise which are worthy of discussion. Jenkins and Drennan[10] report a marked mottling in the position of the upper calix. Gayet, Gabrielle, and Martin[18] report a similar mottled appearance of an upper calix, and in our case now reported there was an irregular mottling in the upper calix which led support to the tentative diagnosis of early tuberculous infection. After the removal of the kidney in our case, the renal pelvis was again injected from the divided end of the ureter with sodium iodide solution, and probably with more tension than would have been used *in vivo*, but a radiographic film showed a normal outline of the bifid pelvis and calices and did not reproduce the mottled effect in the upper calix (*Fig.* 203). We

FIG 203.—Pyelogram of the kidney obtained by injecting the divided ureter with sodium iodide solution after removal. The upper calices do not show the same mottled appearance as in the former pyelogram.

are inclined therefore to look upon this irregularity in the outline as due to adherent blood-clot at the time of the pyelography. In two cases the pyelograph showed no change from the normal, but in four a deformity of the pelvis or of a major calix led to a diagnosis of renal growth.

It is perhaps significant that of the 9 cases in which pyelography was carried out, a bifid pelvis was found in 3, whilst in a fourth case in which a kidney was removed by Kidd[5] a similar condition was present. Whether this abnormality may bear any relation to the presence of an angioma which may be etiologically due to some developmental vascular derangement must remain undecided. Gayet, Gabrielle, and Martin[18] consider that the presence of a bifid ureter would tend to support a suspicion of an embryological tumour in the kidney.

Unilateral renal hæmaturia may occur in association with *increased mobility of the organ*, often coinciding with attacks of acute renal colic or directly following some exertion, and is probably due to passive hyperæmia of the kidney from pressure upon or torsion of the renal vein. These cases must be carefully diagnosed from any form of renal growth, as the renal tissue is healthy and the fixation of the organ into its true anatomical position will effect a cure of the hæmaturia and save the kidney.

Hydronephrosis may occasionally be accompanied by unilateral hæmaturia, but the palpation of an enlarged kidney and the evident dilatation of the renal pelvis or calices on pyelographic examination will make the diagnosis obvious.

A series of cases of *varix of the renal papillæ* causing unilateral renal hæmaturia are described by Fenwick,[19] Newman,[27] Pilcher,[28] and others in which the veins of the papillæ are engorged and dilated and which have a tendency to bleed. These cases are not true angiomata and were cured by extensive nephrotomy and subsequent suture, the thrombosis of the veins by such operative interference arresting the bleeding. In some cases a wedge-shaped resection of the affected papilla was carried out, but the microscopic examination of the portion removed showed only engorged and dilated blood-vessels without any reference to angiomata. Newman, in his article, implies that the condition of renal varix has an entirely separate pathology to that of angioma.

In an article by Kidd[29] 24 cases of *purpura of the urinary tract* are analysed. All showed hæmaturia in varying amounts, and in 5 of these cases it was confined to one kidney, and Kidd suggests that the condition may explain many cases of painless renal hæmaturia. In one case of hæmaturia from vesical purpura, one kidney had been previously removed for unexplained hæmaturia, and in 6 cases in which nephrectomy had to be performed owing to the severity of the renal hæmorrhage, 3 subsequently had mild attacks of hæmaturia. In most cases the hæmaturia is accompanied by a streptococcal infection in the throat, nasal sinuses, teeth, or bowel, or by acute rheumatism, and the blood in the urine may be associated with purpuric areas in the skin or by bleeding from the gums, the nose, or the bowel. Bacteriological examination of the urine may be positive for organisms and the blood may show an absence or diminution of platelets. A case of unilateral renal hæmaturia from purpura of the renal pelvis requiring nephrectomy is reported by Ogier Ward,[30] but in this case no other sign of purpura was present.

In the reported cases of renal angiomata in which the hæmaturia was intermittent or in which it was not so profuse as to demand early operation, renal function tests were carried out by chromocystoscopy, when in every case it is reported that the dye was excreted within normal time limit, which is not surprising considering the very limited lesion usually found in the renal tissue after removal. The fact of a rapid elimination of good colour after an intravenous injection of indigo-carmine might be used as a differential diagnosis, as it is usually impaired quite early in tuberculous disease and often deficient with stone or growth. Where circumstances allow, every possible test should be carried out to estimate the functional efficiency not only of the kidney which has been proved to be bleeding, but also of the remaining kidney in case a nephrectomy may be required. These tests should include chromocystoscopy, intravenous pyelography, and the complete analysis of the urine obtained by ureteric catheterization, preferably carried out one and a half hours after the ingestion of 15 grm. of urea. In many cases, however, the abundance of the hæmorrhage does not allow of extended examination,

and in 13 of the collected cases it is definitely stated that the hæmorrhage was so profuse when the patient came under observation either in his first or in his most recent attack that, having been localized to one kidney, it was deemed inadvisable to delay operation, owing to the profound anæmia.

We feel, therefore, that in any case in which hæmaturia is localized to one kidney, is sudden and profuse, and is free from evidence of stone, tubercle, or growth, a renal angioma should be suspected, particularly in a patient of comparatively early age. We also feel that if complete examination of these cases of unilateral renal hæmaturia is made, the list of cases under the head of ' essential hæmaturia ' will be materially lessened.

TREATMENT

Any discussion on the treatment of renal angiomata is difficult owing to the great rarity of the disease and can only be outlined from general principles. The growth is an innocent tumour and the removal of the whole kidney seems an unnecessary sacrifice. In cases in which tuberculosis, calculus, and growth can be excluded and in which the hæmorrhage is only moderate, such measures as intrapelvic lavage with nitrate of silver or adrenalin might be tried, but where the bleeding is profuse and seems to endanger life, some surgical attack upon the kidney must be considered. The possibility of a malignant growth must be suspected in those cases in which complete pre-operative investigation has been impossible owing to the severity of the hæmorrhage. In such cases it would probably be advisable to proceed to an immediate removal of the kidney, together with the surrounding perinephric fatty tissue, rather than to risk the immediate spread of carcinomatous cells by an exploratory nephrotomy. Such treatment is also to be recommended when the general condition of the patient from profound anæmia will allow neither a prolonged operation nor one which is not certain of arresting the bleeding. In the remaining cases of proved intermittent unilateral renal hæmaturia in which the bleeding is less profuse and in which complete urological investigation has been carried out, growth, tuberculous disease, and calculus can almost certainly be excluded and a direct inspection of the renal pelvis may be undertaken by nephrotomy or by pyelotomy. In such cases a varix of a papilla or an angioma might be removed by endothermic resection and the kidney saved, but such favourable circumstances must be indeed uncommon. In most cases and especially when it is known that the remaining kidney is free from disease and functionally active, nephrectomy seems to offer the best chance of complete recovery.

SUMMARY

1. A further case of cavernous angioma of the renal pelvis is reported.
2. Twenty-six other cases have been collected from the literature.
3. The diagnosis of cases of unilateral renal hæmaturia is fully discussed.
4. The treatment of renal angioma is briefly discussed.

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THROMBOSIS   FOLLOWING   STRAIN

BY R. H. O. B. ROBINSON

SURGEON TO OUT-PATIENTS AND DEPUTY DIRECTOR, SURGICAL UNIT, ST. THOMAS'S HOSPITAL

PRIMARY thrombosis of normal veins in otherwise healthy individuals due presumably to trauma from muscular contraction has attracted considerable attention during recent years.

The vein in which the condition is seen is the axillary as a rule. Not unnaturally from what follows it is the vein of the right side that is usually affected, and the current theories of its causation are: (1) Cadenat's, that venous dilatation due to expiration combined with muscular strain injures the intima of the 'venous tributaries' at their junction with the axillary vein; (2) Lowenstein's, that venous dilatation due to expiration combined with marked abduction of the arm produces indentation of the axillary vein by the costo-coracoid ligament; (3) That of Pearce Gould and Patey, that sudden contraction of the subclavius muscle tears the subclavio-axillary valve in the long axis of the vein, especially in the abducted position of the arm and during marked expiration.

In nearly all the recorded cases a history of trauma could be elicited, and the condition has been called by Cadenat, 'phlébite par effort'. Therefore it might be expected to appear in other veins. Recently I have seen two cases of primary thrombosis, the result of excessive muscular effort, affecting the thoraco-epigastric vein of the right side (*Figs.* 204, 205).

The patients were both healthy and in the prime of life, as is the case in axillary thrombosis, and in both there was little subcutaneous fat, so that the vein was both visible and palpable. In one, a male aged 30, the condition developed after digging in the garden, and in the other, a female, after shifting some heavy furniture. The symptoms were pain felt in the side of the chest wall and the discovery of a tender cord.

On examination a string-like band under the skin running up from the costal margin just behind the breast under the anterior axillary fold and disappearing in the axilla, was palpable and tender. In one of the cases there was obvious discoloration of the overlying skin, in the line of the vein. The physical signs cleared up completely in six weeks. The condition is of clinical interest, particularly in the female sex, because its close relationship to the breast may give rise to confusion in diagnosis.

Anatomically the vein is part of the venous tract represented by the lateral thoracic vein opening into the axillary vein above, the thoraco-epigastric vein, the connecting link, and the superficial epigastric of the abdominal wall below opening into the common femoral. This tract is of prime importance in blocking of either the superior or the inferior vena cava. In the upper part its valves deflect the blood to the axillary vein.

FIG 204 —Infra-red photograph of the thoraco-epigastric vein in a normal subject

FIG 205 —Infra-red photograph showing communication between the common femoral and the lateral thoracic vein in a case of thrombosis of the inferior vena cava

As a cause of thrombosis one can postulate congestion and injury of the venous intima during contraction of the underlying muscles, possibly with injury of the valves in the lumen of the vein.

It is possible that the condition of axillary thrombosis may originate in this vein, the primary thrombosis being overlooked in the major condition affecting the axillary vein, especially as it is unlikely that the patient will draw attention to the original condition.   In this connection both the patients were educated and observant people.

My senior colleague, Mr. C. Max Page, informs me that he has seen quite recently a similar case, but otherwise I am unaware of any record of the condition as a clinical entity.

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THE LATE RESULTS OF OPERATIONS ON THE BILIARY TRACT IN 359 CASES, WITH CHOLECYSTOGRAPHIC STUDIES IN 18 *

By JAMES H. SAINT

SENIOR SURGICAL REGISTRAR, ROYAL VICTORIA INFIRMARY, NEWCASTLE-UPON-TYNE

SINCE the criterion of any operation lies in the ultimate benefit obtained by the patient, the greater the time which has elapsed since its performance, the more reliable the information will be on which to base an opinion of its merits or its shortcomings. It was decided, therefore, before this investigation was begun, that no case coming within its scope should have a post-operative history of less than ten years. In the hope of obtaining results in a number of cases sufficiently large to render justifiable any conclusions which might be drawn therefrom, the investigation was extended to cover the previous fifteen years, so that from ten to twenty-five years have elapsed since the cases in this series were operated upon. All of them were taken from the records of the Royal Victoria Infirmary, Newcastle-upon-Tyne, the honorary staff of which institution I wish to thank for the facilities accorded me.

Early in 1933 questionnaires were sent out to 790 patients who left hospital after having undergone operations on the biliary tract during the years 1907–22. The answers received amounted to 359, these including a considerable number from patients who came to the infirmary and reported to me in person and also communications from relatives or friends of those who had died. Thus about 45 per cent of patients were traced. Through the detailed consideration of these answers, certain statistics become available and later will be presented and discussed at some length.

Interpretation of the results of operation is always a matter of some difficulty, for there is much truth in the cynical observation that statistics can be made to prove anything. While admitting that the amount of benefit obtained is the true criterion of any operation, yet to estimate the relative values of different operative procedures one must have a basis of comparison. This basis must necessarily be the pathology present at the time of operation, for, unless this is the same in each case, results cannot be properly compared. In accordance with this premise, the cases in this series are grouped according to their pathology. The practical limitations to which this theoretically correct arrangement is subject become at once apparent, but, as will be seen, they are unavoidable at the present time. However, in spite of this, it is important that they should be given recognition.

It cannot be over-emphasized that the gall-bladder is not a separate entity

but is only a specialized portion of a particular hollow muscular system, the biliary tract; that by far the greater part of this tract is intra-hepatic and therefore, at operation, is not available for examination. It is difficult to believe and, I think, wrong to assume that if infection is present in the gall-bladder, it will remain limited to that organ and not invade the unseen intra-hepatic portion of the biliary tract.

The ultimate effect of disease of the biliary tract is damage to the parenchymal cells of the liver, with resulting hepatic inadequacy. The condition of the liver, therefore, is of paramount importance in these cases, though little stress seems to have been laid upon it. The extent of any changes which the liver may have undergone cannot be ascertained, nor can the amount of damage it may have suffered be properly assessed. It is true that in the liver adjacent to an infected gall-bladder some degree of hepatitis may be evident. Does this extend beyond its macroscopic limit? We do not know. Does this hepatitis necessarily mean damage to liver function, and, if it does, is the amount of hepatitis proportionate to the degree of liver inadequacy? Again, we do not know. This hepatitis has been cited as an evident sign of liver change and presumably of damage, but if no visible change is present in the liver, can we assume that it has suffered no damage? I would hesitate to answer this question in the affirmative, for it is known that infection can be present in the bile-ducts to a marked degree without accompanying external change in the liver. How, then, are we to determine the amount of damage the liver may have suffered? The unfortunate truth is that until there is introduced a reasonably simple and reliable test for liver function we shall be compelled to forgo this most important knowledge.

Thus it will be seen that, in two given cases classed as acute or chronic chole-cystitis, while the pathological change in each gall-bladder may be similar, the degree of invasion of the infection into the intra-hepatic portion of the biliary tract remains unknown. The consequent damage to liver function in the one case may be considerable, in the other negligible. For this reason the pathological basis of comparison is inadequate and must remain so at present. Moreover, this variation may explain the difference in the clinical results obtained after the same operation in cases where the apparent pathology was similar in degree and extent.

Furthermore, since pathology in other abdominal viscera may give rise to symptoms simulating those of biliary tract disease, it is quite possible that such pathology, having been overlooked at the time of operation on the biliary tract, may have a definite effect on the result obtained.

While these limitations should be borne in mind when considering results of operations on the biliary tract, yet we do not know to what extent they actually affect them. Nevertheless, this is no reason why attention should not be drawn to them, for it is only by their recognition that in due course they may be eliminated.

RESULTS OF OPERATION

These naturally are expressed in terms of the amount of relief obtained by the patient, and I have therefore elected to classify them by division into four groups —those who obtained: (1) Total relief; (2) Partial relief; (3) No relief; and (4) Those who have been subjected to a secondary operation on the biliary tract.

The fourth group consists of cases which, until the secondary operation, belonged to the second and third groups. The performance of the secondary operations, however, calls for the segregation of these cases into a group by themselves.

The use of the word ' cure ' has been purposely avoided, for although many of those who have obtained total relief may actually be cures, yet the words are by no means necessarily synonymous. A true cure should not only mean total relief of symptoms—i.e., symptomatic cure—but should also indicate the absence of pathology similar to, or consequent upon, that for the relief of which the operation was primarily undertaken. For example, it is quite possible that, in a case of symptomatic cure following cholecystostomy, stones have re-formed silently in the gall-bladder. In a similar case after cholecystectomy, small stones may form in the smaller radicles of the biliary tract and pass down the common duct to escape into the duodenum without giving rise to symptoms. While such cases, then, can be grouped under the heading of ' total relief of symptoms ', they are not cures in the true sense of the word and have no right to that name.

I have endeavoured to group the results according to this classification with all possible honesty, although realizing it is just as easy to obtain misleading results by being over-zealous in this respect as it is to do so by disregarding that virtue. The only cases put into the first group are those whose answers were unequivocal ; on the other hand, several patients still complain of flatulence which, after all, might be due to causes other than mild persisting trouble in the biliary tract, yet it is by no means certain that even a full investigation would enable one to discover the etiological factor. However, such cases are regarded as failing to qualify for insertion into the first group. Several more, in the course of many years, have had only one or two attacks of recurrence of symptoms since their operation, with no interval or present symptoms, yet these attacks have precluded them from admission into the ' total relief ' group. I feel that cases of this type sometimes find their way into the category of cures in statistics on this subject, especially if they are reported soon after operation before one of these attacks has occurred. This group of cases forms a subject for later discussion.

With regard to the assignment of cases to the second and third groups, there were a few of the border-line variety, and in these the personal equation was necessarily a factor.

Tables I to *V* are presented below, seriatim, for the convenience of the reader.

It will be seen in *Table I* that the number of cases in which the gall-bladder was removed is unfortunately small in comparison with that in which the organ was drained or closed, but this is no doubt accounted for by the fact that during

Table I.—GENERAL DATA

	GALL-BLADDER REMOVED	GALL-BLADDER DRAINED (OR CLOSED)	TOTALS
Questionnaires sent out	95	695	790
Replies	46	313	359
Died	5	49	54
Surviving cases	41	264	305

Table II.—ANALYSIS OF 305 CASES ACCORDING TO PATHOLOGY PRESENT AND OPERATION PERFORMED

PATHOLOGY	OPERATION	
	Gall-bladder Removed	Gall-bladder Drained (or Closed)
Chronic cholecystitis with cholelithiasis ..	32	204
Chronic cholecystitis without cholelithiasis	0	9
Acute cholecystitis with cholelithiasis ..	9	51

Table III.—RESULTS IN 236 CASES OF CHRONIC CHOLECYSTITIS WITH CHOLELITHIASIS

OPERATION	NUMBER OF CASES	TOTAL RELIEF	PARTIAL RELIEF	NO RELIEF	SECONDARY OPERATIONS
Cholecystectomy ..	31	19 (61·3%)	8 (25·9%)	3 (9·6%)	1 (3·2%)
Cholecystectomy and choledochlithostomy ..	1	1	–	–	–
Cholecystlithostomy ..	177	100 (56·5%)	37 (20·9%)	13 (7·3%)	27 (15·3%)
Cholecystlithostomy and choledochlithostomy ..	18	16 (88·8%)	1 (5·6%)	1 (5·6%)	–
Cholecystlithostomy and choledochostomy ..	2	2	–	–	–
Cholecystlithotomy ..	6	1	4	1	–
Cholecystlithotomy and choledochlithostomy ..	1	1	–	–	–

Table IV.—RESULTS IN 9 CASES OF CHRONIC CHOLECYSTITIS WITHOUT CHOLELITHIASIS

OPERATION	NUMBER OF CASES	TOTAL RELIEF	PARTIAL RELIEF	NO RELIEF	SECONDARY OPERATIONS
Cholecystostomy ..	8	6 (75·0%)	1 (12·5%)	–	1 (12·5%)
Cholecystostomy and choledochostomy ..	1	1	–	–	–

Table V.—RESULTS IN 60 CASES OF ACUTE CHOLECYSTITIS WITH CHOLELITHIASIS

OPERATION	NUMBER OF CASES	TOTAL RELIEF	PARTIAL RELIEF	NO RELIEF	SECONDARY OPERATIONS
Cholecystectomy ..	9	7 (77·8%)	2 (22·2%)	–	–
Cholecystlithostomy ..	49	27 (55·1%)	16 (32·7%)	3 (6·1%)	3 (6·1%)
Cholecystlithostomy and choledochlithostomy ..	2	2	–	–	–

the period of time when these patients were operated upon, cholecystectomy had attained nothing like its present popularity. The deaths which have occurred will be discussed later.

From *Table II* it will be seen that of the 305 surviving patients there were only 9 (3 per cent) in whom stones were not found, chronic cholecystitis being the only pathology noted. There were no cases of acute cholecystitis without cholelithiasis, stones being present in the 60 in whom the gall-bladder was acutely inflamed.

The percentages of those who have obtained total relief of symptoms following operation, as seen in *Table III* (61·3 per cent after cholecystectomy and 56·5 per cent following cholecystostomy), appear to be rather low when compared with some others in the literature. Some of the probable reasons for this have already been indicated. However, if the percentages of patients who have received partial relief are added to those above, we find that 87·2 per cent following cholecystectomy and 77·4 per cent following cholecystostomy have been benefited by operation. These results, then, are not so unfavourable as they might appear at first sight.

While the percentages of those who obtained no relief from either of these operations are much the same, there is a striking difference in those representing cases which have come to secondary operation, there being 15·3 per cent after drainage of the gall-bladder and only 3·2 per cent following its removal. It is obvious, therefore, that the morbidity after cholecystostomy was considerably greater than that following cholecystectomy. The secondary operations performed on cases of this series form a subject for consideration later.

Those patients in whom the gall-bladder was closed after the removal of stones are only 6 in number; 5 of these have benefited by the operation, though only 1 has obtained total relief of symptoms. Although this operation is not often performed, yet it obviously has its uses, particularly in cases where the stones are of pure cholesterin and therefore metabolic in origin and the gall-bladder looks normal or only a very mild degree of chronic infection appears to be present in its wall.

Of the greatest interest are the results in those patients in whom the operative procedure on the gall-bladder was combined with drainage of the common duct. This latter operation was performed in 20 patients in whom the gall-bladder was drained, in 1 in whom that organ was closed after the removal of stones, and in another in whom cholecystectomy was done. Of the 21 patients in whom the gall-bladder was not removed, 19 (90·5 per cent) have obtained total relief of symptoms. The patient in whom drainage of the common duct was combined with cholecystectomy has also been completely relieved of symptoms. These results are so much better than those which followed only removal or drainage of the gall-bladder that it is important to investigate the factors responsible for their production. It was emphasized in a previous paragraph that the gall-bladder should not be regarded as a separate entity but considered as a portion of the biliary tract; that, in consequence, when the gall-bladder is the seat of an infection, this has probably also involved the unseen intra-hepatic portion of the tract in greater or less degree. It would seem, therefore, that either cholecystostomy or cholecystectomy is an inadequate procedure to deal efficiently with the pathology present, for is it to be expected that either of these operations alone can be productive of the best results when nothing is done to combat the infection in the intra-hepatic portion

of the tract and it is left behind as a residuum? We know that the principle underlying the treatment of infection of any hollow muscular system is the provision of adequate drainage. Where cholecystostomy has been performed, it is true that a drainage has been provided, but a valved and pathological cystic duct is liable to possess limitations as a channel for the unimpeded outflow of bile; direct proof of this lies in the fact that the daily amount of bile drained by cholecystostomy is considerably less than that in a case of common-duct drainage. On the other hand, where cholecystectomy has been done, no drainage at all has been provided for the infection lurking in the intra-hepatic radicles of the biliary tract. How, then, is adequate drainage of this portion of the biliary tract to be effected? Surely by drainage of the common duct, and this, I consider, satisfactorily explains the excellent results in this group of cases.

It is of interest that choledochlithiasis was present in 20 of these 22 cases, for a stone in the common duct is a complication which, by causing obstruction, leads to back-pressure and predisposes to infection of the obstructed bile. The resulting damage to the liver, however slight, cannot but have a detrimental effect on the individual and adversely affect the prognosis. It is impossible to say to what extent the liver was damaged in the cases under review, for even to-day we still have no means of measuring the degree of damage to the liver resulting from such a complication. The fact remains, however, that those cases in which its effects were combated on sound principles—namely, the removal of the obstruction and the provision of adequate drainage—have proved to be the most successful of the present series.

While the number of patients in whom stones were not found is small, as seen in *Table IV*, the percentage of those who obtained total relief of symptoms is definitely higher than in those cases with cholelithiasis. This is really to be expected, for cases such as the former no doubt represent an earlier stage of the disease. Hence these results seem to indicate that the sooner operation is undertaken the better will be the prognosis. Another patient is seen in this table in whom the common duct was drained and who has enjoyed total relief of symptoms since the operation.

The results in the small number of acute cases treated by cholecystectomy (*Table V*) are much better than those of the chronic cases treated by the same procedure. All patients are definitely improved and 77·8 per cent have obtained complete relief. These results are also much better than those in the same type of case treated by cholecystostomy.

A comparison of acute and chronic cases with cholelithiasis treated by drainage of the gall-bladder shows that, while the percentage of those who have obtained total relief of symptoms is about the same (55·1 per cent in acute cholecystitis and 56·5 per cent in chronic cholecystitis), yet that of cases with partial relief is considerably higher in the acute group. Consequently, we see that relief in some measure was obtained by 87·8 per cent of acute cases as compared with 77·4 per cent in which chronic infection was the pathology present. A possible explanation of these results may be as follows: in most cases of acute cholecystitis the gall-bladder shows a marked distension such as could not occur were the wall of the organ the seat of widespread fibrotic change. Since such change is the result of a chronic inflammation, it follows that most cases of acute cholecystitis occur at a relatively early stage of the disease.

In this table are a further two patients in whom the common duct was drained and who have obtained total relief of symptoms. This brings the total number of such cases in this series up to 25; of these, 23 (92 per cent) have obtained total relief, and 1 has obtained partial relief, bringing the percentage of those obtaining relief in greater or less degree up to 96. Such results are excellent.

ANALYSIS OF CASES WITH PARTIAL RELIEF AFTER OPERATION

First will be considered those patients in whom the gall-bladder was allowed to remain. They number 59, and the gall-bladder was drained in all except 4, in whom it was closed after the removal of stones. *Table VI* shows the time of recurrence of symptoms in these cases. In 8 cases, in spite of further inquiries, the answers received regarding the time of recurrence of symptoms were too indefinite to allow of their inclusion in this table.

Table VI.—TIME OF RECURRENCE OF SYMPTOMS AFTER CHOLECYSTOSTOMY IN 51 PATIENTS

TIME AFTER OPERATION	NUMBER OF CASES	TIME AFTER OPERATION	NUMBER OF CASES
Years		Years	
1	9	11	3
2	3	12	2
3	4	14	4
5	3	15	1
6	2	16	1
7	6	17	5
9	2	20	2
10	4		

An arresting feature of this table is that no fewer than 18 of these 51 cases, whose time of recurrence of symptoms is known, were well for ten years after their operation and therefore, up to this time, could have been grouped under 'total relief' or regarded as cures by those who adopt that nomenclature. These figures demonstrate well the fallacy of accepting results published too soon after operation.

There was mentioned previously the occurrence of a certain type of patient who, following an operation on the biliary tract, may have one or two subsequent attacks, at long intervals, of trouble suggestive of the recurrence of biliary tract disease, with complete remission of symptoms between the attacks, which apparently finally cease and leave the patient perfectly well. Eleven of the cases in *Table VI* belong to this category, and the details of their post-operative histories are disclosed in *Table VII*.

From a consideration of *Table VII*, the important question arises as to the pathology underlying these attacks. One most readily concludes that stones have formed again and that their attempted extrusion from the biliary passages is the source of trouble. There are three reasons, however, which tend to render invalid this explanation. In the first place, the great length of the intervals between the attacks is not characteristic of cholelithiasis. Secondly, the intervening freedom from symptoms is unlike the behaviour of gall-stones with their concomitant

chronic cholecystitis. Thirdly, and most important, in cases of this nature no evident pathology may be found on exploration. Since *the* cause of biliary colic is obstruction to the outflow of bile, it is suggested, because of the reasons mentioned above, that the cause of the obstruction in these cases is some factor consequent upon a transitory inflammation of the biliary tract, such as œdema or plugs of inspissated mucus or epithelial debris.

Table VII.—Post-operative History following Cholecystostomy
in 11 Patients

Number of Case	Year of Operation	Post-operative History
1	1909	Biliary colic with jaundice 15 years after operation; a second attack 9 years after the first (early 1933); no other symptoms
2	1910	Biliary colic 17 years after operation; no previous or subsequent post-operative symptoms
3	1910	*Biliary colic about 6 months after operation; no other* symptoms
4	1916	Biliary colic 16 years after operation; no other symptoms
5	1917	Pain and flatulence " very bad " for 2 years after operation; no other symptoms
6	1917	Three attacks of biliary colic, first 6 months after operation, last in 1930. No symptoms between attacks; now perfectly well
7	1918	Gall-stone colic 11 years after operation; no other symptoms
8	1918	Biliary colic in 1931; no other symptoms
9	1921	Eight months after operation had intermittent pain and jaundice for 6 weeks; no other symptoms
10	1921	Pain, vomiting, and jaundice in 1924; similar attack in 1925; no other symptoms
11	1921	Biliary colic with jaundice in 1926; no other symptoms

It is important that wide recognition should be given to this type of case in order that unnecessary exploratory operations may be avoided. Because such cases do occur, it would seem that, where there is a post-operative recurrence of symptoms, be it early or late after operation, a policy of " wait and see " should be adopted, for there may be a return to the previous state of good health once the attack has subsided.

Table VIII.—Time of Recurrence of Symptoms after Cholecystectomy
in 10 Patients

Time after Operation	Number of Cases	Time after Operation	Number of Cases
Years		Years	
1	4	11	1
3	1	16	1
4	1	20	1
9	1		

Concerning the symptoms complained of by these 59 patients, it was found that, while in 11 flatulent dyspepsia alone was present, and pain, vomiting, jaundice, and flatulence occurred together only in 3, *the remaining 45* presented

various combinations of these symptoms. Actually, pain was the most frequent, occurring in 40, while in decreasing order of frequency there was vomiting in 35, dyspepsia in 19, and jaundice in 12.

The cases of this group in which the gall-bladder was removed are 10 in number. *Table VIII* shows the time of recurrence of their symptoms after operation.

Table VIII shows that 3 of these 10 cases were well for at least ten years following operation, and the remarks made previously concerning the 18 cases in *Table VI* apply also to these 3.

There is again evidence of a group of cases with a post-operative history of attacks, indicative of biliary tract disease, occurring at long intervals with intervening remission of symptoms. They are 6 in number and the details of their post-operative histories are given in *Table IX*.

Table IX.—POST-OPERATIVE HISTORY FOLLOWING CHOLECYSTECTOMY
IN 6 PATIENTS

NUMBER OF CASE	YEAR OF OPERATION	POST-OPERATIVE HISTORY
1	1908	Jaundice, lasting 5 to 6 months, beginning 6 months after operation; no other symptoms
2	1910	Biliary colic with jaundice in 1926; similar attack in 1932; no other symptoms
3	1913	Nine months after operation, intermittent pain and jaundice lasting 6 months; no other symptoms
4	1921	Biliary colic in 1930 followed by dyspepsia for some weeks; no other symptoms
5	1922	Biliary colic 3 months after operation; no other symptoms
6	1922	Biliary colic with jaundice in 1926 and 1932; no other symptoms

Since all these cases had their gall-bladders removed, the possibility of their isolated attacks being due to the passage of stones seems less likely than in those cases where the gall-bladder was only drained, for calculus formation in the liver is of comparatively infrequent occurrence. Should the condition of the liver be such as to favour this, one would expect a repetition of attacks of colic at short intervals. Because of the rarity of the attacks in these cases, it would seem that we must look for some other causative factor and it is suggested that this also is obstruction consequent upon a transitory inflammation of the biliary tract. Again, the advisability is obvious of adopting a " wait and see " policy in such cases.

The most frequent symptom complained of by these 10 patients was pain, which occurred in 8; vomiting was the next most frequent, occurring in 6 patients; and 4 have suffered from jaundice and flatulence.

ANALYSIS OF CASES WITH NO RELIEF FOLLOWING OPERATION

The patients in this group on whom a cholecystostomy was performed are 18 in number, and *Table X* shows the times of recurrence of their symptoms.

Since all these cases began to have recurrence of their symptoms within three years after operation, such early return of symptoms would seem to indicate that they are more likely to persist.

Table X.—TIME OF RECURRENCE OF SYMPTOMS AFTER CHOLECYSTOSTOMY
IN 18 PATIENTS

TIME AFTER OPERATION	NUMBER OF CASES
Years	
1	13
2	3
3	2

Of these 18 patients, all complained of attacks of pain and vomiting; jaundice has been present at one time or another in 7; and 12 have suffered from flatulence.

Passing to the patients in whom cholecystectomy was performed, we find that there are only 3. Symptoms recurred in all within a year after operation. All have suffered from attacks of pain and vomiting, 2 of them from dyspepsia, but jaundice has not occurred in any.

ANALYSIS OF DEATHS WHICH OCCURRED AFTER RECOVERY FROM OPERATION

In this series there are 54 patients who have died since leaving hospital; the causes of death were ascertained in 43 cases and they are given in *Table XI*.

Table XI.—CAUSES OF DEATH OF 43 PATIENTS AFTER RECOVERY FROM OPERATION

CAUSE OF DEATH	OPERATION PERFORMED	
	Cholecystostomy	Cholecystectomy
Cardiovascular disease :—		
Heart disease	7 } 9	1 } 2
Apoplexy	2	1
Carcinoma :—		
Œsophagus	4	
Stomach	1	
Colon	1 } 11	
Breast	1	1
Penis	1	
Affected organ unknown	3	
Pneumonia	2	—
Lung abscess	1	—
Pulmonary tuberculosis	1	—
Gastric ulcer	1	—
Ruptured peptic ulcer	1	—
Acute appendicitis	2	—
Diabetes	2	—
Subacute pancreatitis	1	—
Tuberculosis	1	—
Rheumatic fever	1	—
Renal disease	1	—
Strangulated hernia	2	—
Exophthalmic goitre	1	—
Cerebral tumour	1	—
Childbirth	1	—
'Eye trouble'	1	—

In 3 other cases the cause of death was stated to be "in no way connected with the operation."

From *Table XI* it will be seen that, while the causes of death are many and varied, carcinoma was responsible for 12 and cardiovascular disease for 11. It is of interest that the gall-bladder was not involved in the 9 cases of carcinoma in which the organ affected is known. One of the arguments put forward by the advocates of cholecystectomy is that an infected gall-bladder which has been drained is a potential focus of carcinoma. In the few cases of cancer of the gall-bladder upon which I have operated, the organ had not been previously subjected to operation, and I believe this to be the usual experience in abdominal surgery. While admitting that carcinoma does occur in gall-bladders which have been drained, the figures above seem to indicate that its incidence in these cases is certainly no greater than in those in which the organ has not been subjected to this surgical procedure. For this reason I feel that the fear of the onset of carcinoma should not be acknowledged as a valid objection to drainage of an infected gall-bladder.

Seven of the deaths of patients in whom cholecystostomy had been performed were due to heart disease, and the question arises of the possibility of these pathological gall-bladders having persisted as chronic foci of infection with a resulting myocarditis through systemic infection. Rosenow, of the Mayo Clinic, has satisfied himself that cultures of streptococci isolated from the walls of infected human gall-bladders are capable of producing myocarditis when injected into experimental animals. Further, it is known that in some instances systemic infection has cleared up following the removal of an infected gall-bladder—apparently examples of cause and effect. On the other hand, against the assumption that the gall-bladders in these 7 cases might have persisted as foci of infection there is certain clinical evidence, for it was reported in 4 that the operation was regarded as having been a perfect success during the time of the patient's post-operative survival. Again, the middle and late periods of life during which gall-bladder disease is prevalent are also those in which heart lesions manifest themselves. For these reasons, it does not seem justifiable to regard the drained gall-bladder as the essential etiological factor responsible for the heart disease in the above cases.

The baneful effect of disease of the biliary tract on the pancreas, although ordinarily given much prominence, does not appear to have been unduly detrimental in this series of cases. Pancreatitis was the cause of only 1 death and diabetes of 2. While admitting that the former might have been due to infection from the biliary tract, the incidence of diabetes amongst individuals who have no lesion of this tract is so great that its occurrence in these 2 cases must be regarded as much in the nature of a coincidence as an example of cause and effect.

The causes of death of the remaining 17 cases do not appear to bear any definite relationship to the infection of the gall-bladder for which the patient had been previously subjected to operation.

Inquiries were instituted to ascertain the length of post-operative survival of these 54 patients and their state of health during this period. *Table XII* shows the results of the first part of the inquiry.

From *Table XII* it will be seen that of the 49 patients in whom cholecystostomy was performed, 25 lived for at least ten years after operation, while of the 5 who had their gall-bladders removed, 3 survived longer than this period.

The results of the inquiry into the post-operative state of health of these patients are shown in *Table XIII*. It was ascertained in 33 cases only.

In the 9 patients in whom symptoms recurred, the data obtained were insufficient to enable them to be subdivided into the groups of partial or no relief.

Table XII.—LENGTH OF POST-OPERATIVE SURVIVAL OF 54 PATIENTS

YEARS AFTER OPERATION	OPERATION PERFORMED		YEARS AFTER OPERATION	OPERATION PERFORMED	
	Cholecystostomy	Cholecystectomy		Cholecystostomy	Cholecystectomy
1	4	–	11	4	1
2	3	1	12	2	–
3	1	–	13	1	–
4	2	–	14	5	1
5	3	–	15	4	–
6	2	–	16	1	–
7	1	–	17	2	–
8	1	–	18	2	–
9	1	–	19	1	–
10	6	1	20	1	1
			22	2	–

Table XIII.—POST-OPERATIVE HEALTH OF 33 PATIENTS WHO EVENTUALLY DIED

OPERATION PERFORMED	POST-OPERATIVE HEALTH	
	Total Relief	Recurrence of Symptoms
Cholecystostomy	21	8
Cholecystectomy	3	1

The correlation of the information contained in *Tables XII* and *XIII* is not without interest. Of the 21 cases in whom *cholecystostomy* had resulted in total relief of symptoms, the time of death after operation varied from two to twenty-two years and no fewer than 12 had a post-operative survival of over ten years. The 3 patients on whom cholecystectomy had been performed with resulting total relief of symptoms lived for 11, 14, and 20 years respectively after their operations.

ANALYSIS OF SECONDARY OPERATIONS

The operations referred to under this heading are those which were performed only for a recurrence of symptoms similar to those for which the primary operation was undertaken. Since, from the point of view of the patient, the necessity of a second operation is a serious consideration, this group of cases is of the greatest importance.

There were 32 patients who had secondary operations performed; the first operation in 31 of these was cholecystostomy and in 1 cholecystectomy. Thirty-four operations were performed on these 32 patients, one of them having been

operated upon on three occasions for choledochlithiasis. The details concerning these cases are shown in *Table XIV*. Several aspects of this group present themselves for consideration and will be discussed forthwith.

Recurrence of Symptoms.—This took place from three weeks to twenty-one years after the first operation. In 14 cases symptoms recurred within one year, and within three years in an additional 7 cases. Four patients were perfectly well for at least ten years after their operation, one of these not having a recurrence of symptoms until twenty-one years had elapsed. Here, then, we again find evidence of a number of patients who obtained total relief from symptoms for at least ten years, although some subsequent development has arisen to prevent them from qualifying for inclusion in the 'total relief' group of the present series.

Pathology.—This, unfortunately, has not been reported fully in many cases, but certain data are available for consideration. In 7 patients the condition of the gall-bladder at both primary and secondary operations was noted. In 2 acute cases (*Cases* 13, 18), at the first operation it was distended, thickened, acutely inflamed, and contained stones ; at the second operation in one of these patients (*Case* 13) it was found to be contracted and fibrosed and contained stones, while in the other (*Case* 18) it was healthy-looking and no stones were present. In 5 chronic cases the gall-bladder, at the first operation, was distended, thickened, and contained stones ; at the second operation its condition was unchanged in 3 (*Cases* 7, 26, 28) and in the other 2 (*Cases* 10, 31) it had become contracted and fibrosed ; stones, however, were present in only 3 of these cases at the second operation (*Cases* 7, 10, 28), being absent in one case where the condition of the gall-bladder was unaltered (*Case* 26) and in another in which the organ had become contracted and fibrosed (*Case* 31). These details appear to indicate that, while acute inflammation in a gall-bladder may undergo resolution, the probability of a chronic inflammation doing so is unlikely. In the latter instance the best that probably can be hoped for is natural cure by fibrosis, but the fact that stones were found again is presumptive evidence that the chronic inflammation was still persisting up to the time of the secondary operation in some of these cases.

Calculi were found in 31 of the 32 patients at the primary operation, being present in the gall-bladder on 30 occasions, and on another in the common duct. At the secondary operations calculi were found in 20 cases, 16 times in the gall-bladder and on 6 occasions in the common duct (three times in the same patient—*Case* 18). In the remaining 12 cases the absence of calculi is reported in 6, while in the other 6 their presence or absence was not noted. The discovery of calculi at a secondary operation on the biliary tract always raises the question of the 'missed' stone and of the extent to which it is responsible for the recurrence of symptoms. In many instances it is very difficult to know whether a stone found at secondary operation is one that was overlooked at the primary operation or one that has formed anew. In this respect the time relationship between pregnancy and the formation of calculi may be helpful, for clinical evidence shows that these can form within the nine months period of cyesis, so that if more than a few months elapse between operations a stone found at the second operation may be one of new formation ; other considerations having some bearing on this problem are the size and number of the stones and, in the case of a single stone, the presence or absence of facets. Attention is drawn to 3 cases whose recurrence of symptoms was probably due to calculi which had escaped the

Table XIV.—Analysis of Secondary Operations

Following Primary Cholecystostomy—

Number of Case	Date of First Operation	Pathology found at First Operation	Time of Recurrence of Symptoms after First Operation	Date of Secondary Operation	Pathology found at Secondary Operation	Operation Performed	Result of Secondary Operation
1	1907	Stones in gall-bladder. None in ducts	12 years ..	1922	Adhesions. Gall-stones present. None in ducts	Cholecystectomy ..	Mild stomach trouble since
2	1909	Stones in gall-bladder. None in common duct	21 years ..	1930	Pocket of pus under scar. Gall-bladder not found	Drainage ..	No further trouble
3	1910	Stones in gall-bladder. None in common duct	1 year ..	1915	Large number of stones in gall-bladder	Cholecystlithostomy	Several attacks of pain since
4	1910	Many adhesions. Stones in gall-bladder	1 year ..	1912	Large chronic duodenal ulcer. Many adhesions in gall-bladder area	Posterior gastro-enterostomy	Fistula developed in 1913. Closed after few weeks. Pains at intervals ever since
5	1911	Stones in gall-bladder ..	16 years ..	1928	Numerous stones present in gall-bladder	Cholecystlithostomy	No further trouble
6	1911	Stones in gall-bladder ..	2 years ..	1922	One stone in gall-bladder	Cholecystectomy ..	No further trouble
7	1912	Gall-bladder distended and thickened. Evident signs of chronic cholecystitis. Numerous small stones in gall-bladder	Not known ..	1927	Multiple adhesions. *Gall-bladder distended and thickened—about 20 stones*	Cholecystogastrostomy	No further trouble
8	1913	Stones in gall-bladder ..	18 months ..	1925	Stones in gall-bladder, which showed thickening	Cholecystectomy ..	No further trouble
9	1913	Many small calculi in gall-bladder	16 years ..	1932	Gall-bladder small and shrunken; many adhesions. No stones in gall-bladder or ducts. Stomach and duodenum healthy	Separation of adhesions	Of benefit
10	1913	Gall-bladder distended and thickened. One stone present. None in ducts	"Shortly after"	1917	Gall-bladder contracted and fibrosed. Five stones found	Cholecystlithostomy	Attacks of pain at intervals. Further operation refused because of diabetes
11	1913	Gall-bladder wall thickened. Stones removed	2 years ..	1917	Gall-stones in gall-bladder. Encysted small *pericholecystic*	Cholecystlithostomy and evacuation of *abscess*	Free from pain for 6 years. Since then pain at

	Year		Duration	Year		Operation	Result
12	1914	Stones in gall-bladder. None in ducts	10 years ..	1925	Gall-bladder embedded in dense adhesions. Small amount of clear bile in gall-bladder. No stones	Cholecystectomy ..	Only trouble since was one attack of pain in 1928
13	1915	Gall-bladder distended, thickened, and acutely inflamed. Containing purulent bile and stones	9 years ..	1931	Gall-bladder small, contracted, and fibrosed. Stones present	Cholecystectomy	No further trouble
14	1916	Stones in gall-bladder ..	4 months ..	1925	Distended gall-bladder, surrounded by dense adhesions	Cholecystectomy ..	No further trouble
15	1916	Stones in gall-bladder ..	8 years ..	1924	Adhesions. Gall-bladder chronically inflamed. Single stone blocking the cystic duct	Cholecystectomy ..	Still has periodic attacks
16	1916	Two stones in gall-bladder	Fistula for 6 months	1917	No pathology noted ..	Cholecystectomy ..	No further trouble
17	1919	Gall-bladder acutely inflamed and containing stones	3 years ..	1932	Gall-bladder containing mucin and many minute stones	Cholecystectomy ..	No further trouble
18	1919	Gall-bladder distended, oedematous, and inflamed. Bile purulent. Stones present	"Within a year"	1920	Gall-bladder healthy-looking. Two stones in dilated common duct	Choledochostomy	Now in good health
				1920	Two stones in common duct	Choledochostomy	
				1921	Gall-bladder flaccid. Wall somewhat thickened. Two stones in common duct	Choledochostomy	
19	1919	Single stone in gall-bladder	Not known ..	1923	Two stones in gall-bladder. Many adhesions	Cholecystlithostomy	No improvement. Much vomiting and pain
20	1920	Stones present in normal looking gall-bladder. No stones felt in common duct	3 weeks ..	1921	Adhesions. Small stones found in gall-bladder. None in common duct	Cholecystectomy ..	No further trouble
21	1921	No stones in gall-bladder. Stones in common duct, which was dilated to about 1 in. in diameter	3 years ..	1924	Gall-bladder shrivelled up. No stones. Common duct dilated. Stones in common duct	Choledochostomy	No further trouble
22	1921	Gall-bladder enlarged and tense. Many stones	2 years ..	1924	Adhesions. No stones in gall-bladder ..	Cholecystectomy ..	Still has attacks of pain and vomiting
23	1921	Gall-bladder containing stones	2 years ..	1923	Not known	Laparotomy ..	Of benefit

Table XIV.—Analysis of Secondary Operations, *continued*

Number of Case	Date of First Operation	Pathology found at Operation	Time of Recurrence or Symptoms after First Operation	Date of Secondary Operation	Pathology found at Secondary Operation	Operation Performed	Result of Secondary Operation
24	1921	Stones in gall-bladder ..	4 months	..	1929	Adhesions between pylorus, gall-bladder, and anterior abdominal wall. Gall-bladder normal looking. No pyloric stenosis	Separation of adhesions	No benefit
25	1921	Gall-bladder surrounded by adhesions. Large number of stones. Pancreas normal	3 months	..	1921	Gall-bladder small and difficult to define owing to adhesions. Stone in cystic duct	Cholecystectomy ..	Has attacks from time to time
26	1922	Gall-bladder dilated and containing stones. Walls slightly fibrotic and thickened	2 months	..	1922	Gall-bladder thickened and dilated. No stones. Adhesions present	Cholecystostomy ..	No further trouble
27	1922	Gall-bladder small. Stones present	" Few months "	..	1922	One stone in gall-bladder	Cholecystostomy ..	No further trouble
28	1922	Gall-bladder distended. Walls slightly thickened. *One stone*	" Few months "	..	1924	Gall-bladder distended and thickened. Soft stones and inspissated bile	Cholecystostomy ..	Still trouble with vomiting and occasional jaundice
29	1922	Gall-bladder distended ; numerous adhesions. No stones	7 months	..	1924	Adhesions present. Stone in common duct. No ulcer in stomach or duodenum. No stones in gall-bladder	Choledochlithostomy	Still has occasional trouble
30	1922	Gall-bladder small and contracted containing putty-like stones. None in common duct	8 years	..	1931	Not known	" Operation on gall-bladder "	Still has occasional trouble
31	1922	Gall-bladder distended and containing stones. Walls thickened	3 months	..	1933	Gall-bladder contracted and fibrosed. No stones. Many adhesions	Cholecystectomy ..	No further trouble

Following Primary Cholecystectomy

Number of Case	Date of First Operation	Pathology found at Operation	Time of Recurrence or Symptoms after First Operation	Date of Secondary Operation	Pathology found at Secondary Operation	Operation Performed	Result of Secondary Operation
1	1916	Gall-bladder wall white and firm. Many stones present	6 years	..	1929	Large stone in common duct	Choledochlithostomy	No further trouble

vigilance of the surgeon at the primary operation. In all these cases (*Cases* 20, 25, 16) stones were found in, and removed from, the gall-bladder at the first operation. In *Case* 20 symptoms recurred three weeks afterwards, and at the second operation, six months later, stones were found again. In *Case* 25 recurrence of symptoms took place in three months, and at the second operation, six months after the first, a stone was found in the cystic duct. *Case* 16, in which a fistula persisted after cholecystlithostomy until a secondary operation was undertaken six months afterwards, was probably also one of missed stone, but unfortunately no note was made of the pathology found at the second operation when the gall-bladder was removed. Another case (*Case* 29) deserves mention here ; no stones were found at the first operation when cholecystostomy was performed, but symptoms recurred in seven months, and at the second operation, two years after the first, a stone was found in the common duct. This case leaves one wondering whether the stone was not overlooked at the first operation through the failure of the surgeon to explore the common duct.

Case 26 is of interest in view of the previously mentioned type of case in which a recurrence of symptoms takes place only to pass away and leave the patient perfectly well. Stones were found and removed at the first operation ; recurrence of symptoms took place in two months and a second operation was undertaken six months after the first. The gall-bladder had not undergone any change and no stones were present. It was again drained and the patient has had no further trouble. The absence of pathology at the second operation and the subsequent good health of the patient lead one to think that the operation was undertaken perhaps unnecessarily.

The discovery of a large, chronic duodenal ulcer at secondary operation in *Case* 4, one year after cholecystostomy, provides evidence of the ease with which other pathology may be overlooked if not specially sought for, as it is almost a certainty that the ulcer was present at the time of the first operation. Its discovery also clouds the issue as to whether or not the gall-stones were the cause of symptoms in the first instance.

In the single case of secondary operation following cholecystectomy, a large stone was found in the common duct. The clinical features of the case—recurrence of symptoms as late as six years after the first operation and the lapse of another seven years before further exploration—seem on the whole to point to the stone being one of new formation. On the other hand, it is not impossible that its formation may be explained by the gradual augmentation of a small stone which was present in the unexplored common duct at the time when cholecystectomy was performed.

Perusal of the foregoing paragraphs makes it clear that the predominant pathology found at the secondary operations was cholelithiasis, characterized mostly by the re-formation of stones in the gall-bladder, although in at least three cases the calculi probably had been left behind at the first operation. In a small group chronic cholecystitis existed unassociated with stones. Cholecochlithiasis, pericholecystic abscess, and duodenal ulcer were also observed. The presence of adhesions was reported in many cases ; in two (*Cases* 9 and 24), at the secondary operation, the separation of these was all that was done. Since adhesions must form in every, or nearly every, case, including those which are completely relieved, it seems unlikely that they, *per se*, are the cause of a return of symptoms.

Clinical Histories following Secondary Operations.—It is important to know the amount of relief obtained from the second operation, and particularly is this knowledge of interest where the two operations differed in type. The details, such as are known, are to be seen in *Table XIV*, but they will be best appreciated by summarizing them.

Cholecystectomy was performed in 13 cases. Since operation, 8 (61·5 per cent) have obtained total relief of symptoms; 3 of these have a post-operative history of ten years of more, 2 of five to ten years, and 3 of under five years. Another patient reports " only trouble was one attack of pain in 1928 " (three years after operation); a second, " mild stomach trouble ever since " (operation eleven years ago). Thus we may consider that 10 cases (77·0 per cent) of the 13 in which secondary cholecystectomy was performed have received relief from the operation. The remaining 3 of these cases still have a fair amount of trouble with periodic attacks of pain.

The 8 patients in whom the secondary operative procedure was cholecystostomy have not progressed nearly so well as those mentioned above after cholecystectomy. Three only (37·5 per cent) have obtained total relief of symptoms, 2 of these having a post-operative history of over ten years, while in the third, five years have elapsed since the second operation. The remaining 5 of these cases appear to have obtained little or no relief from their secondary operations, although 1 (*Case* 11) had freedom from symptoms for six years before they returned.

Choledochlithostomy was performed on 4 patients, 1 having had primary cholecystectomy and the others cholecystlithostomy. The first-mentioned has had no further trouble; of the second group of 3, 1 has obtained total relief of symptoms, another " still has occasional trouble ", and the third, from whose common duct stones were removed on three occasions, reports that she is now in good health.

The meagre report on the pathology present in the patient in whom cholecystogastrostomy was done (*Case* 7) does not make clear the reasons why that particular operation was indicated. The patient, however, has experienced total relief of symptoms during the five years which have elapsed since the operation.

Separation of adhesions was done in two patients, in one with only partial relief, in the other with none. These results tend to confirm my belief that adhesions alone are not likely to be the cause of recurrent symptoms.

The few remaining cases do not present any features of particular interest.

THE EFFECT OF LENGTH OF OBSERVATION ON RESULTS OF OPERATION

So often in the literature one finds operative results compared with each other irrespective of the length of time of post-operative observation. The effect of taking this factor into consideration is strikingly brought out in the present series. There is also a natural tendency to accept the best results, invariably those of cases with a short post-operative history, as those which obtain in general, this giving rise to false impressions of the true value of operation and leading to future disappointments in practice.

On several occasions in the preceding pages attention has been drawn to patients who, although they are not included in the present group comprising those who have obtained total relief of symptoms, yet were in that category for ten

years following operation. The effect of incorporating these cases into the present results, and thereby obtaining results over a ten-year period only, is shown below.

Consider first the results up to the end of ten years in those 264 surviving patients (*Table I*) in whom the gall-bladder was drained or closed. There are 156 (*Tables III–V*) who have obtained total relief of symptoms since their operation, a percentage of 59·1. To these must be added those others who obtained total relief for ten years—namely, 18 of those who are at present grouped under 'partial relief' (*Table VI*) and 4 of those who came to secondary operation (*Table XIV*), making a total of 178 patients who were free from symptoms for ten years following operation. This number represents a percentage of 67·4—that is, 8·3 per cent greater than that when the period of observation was extended to cover twenty-five years.

Similarly, the results up to the end of ten years in patients in whom the gall-bladder was removed are as follows : to the 27 cases grouped under 'total relief' of symptoms (*Table III, V*) must be added 3 from the group of 'partial relief' (*Table VIII*), making a total of 30 cases free from symptoms at the end of ten years after operation. Since the number of surviving cases is 41 (*Table I*), the percentages represented by 27 and 30 cases are 65·9 and 73·2 respectively, a difference of 7·3 per cent in favour of the results for the shorter period of observation.

Five-year results are still better, and, when worked out on a similar basis to those above, it is found that the percentages of those surviving patients who obtained total relief of symptoms up to the end of this time are 74·2 and 78·0 for cholecystostomy and cholecystectomy respectively, representing increases of no less than 15·1 and 12·1 per cent over the corresponding figures when the period of post-operative observation was ten to twenty-five years.

It was seen (*Tables XII, XIII*) that several patients who eventually died lived for more than ten years after operation with total relief from symptoms. They were not included in the calculations above, however, for their number is small compared with that of the surviving cases and thus they would have made no material difference to the percentages obtained.

These figures indicate that we must not be content with a relatively short period of post-operative observation if the value of an operative procedure is to be properly assessed.

THE RELATIONSHIP OF LENGTH OF HISTORY TO RESULTS OF OPERATION

The possibility of the existence of such a relationship is worthy of investigation. In those patients in whom the gall-bladder was drained and whose pre-operative histories were recorded, 147 in number, it is interesting to find that of those who obtained total relief of symptoms 66 per cent had a pre-operative history of under one year ; in those who obtained partial relief, only 38 per cent had a history of similar short duration; while of those who obtained no relief, no patient had a history of less than one year. In the cases of cholecystectomy, pre-operative histories recorded in 19 cases, the percentages for corresponding groups were 60, 25, and 0. These figures seem to indicate that a definite relationship does exist between the length of history and the result obtained, and that the sooner operation is performed following the onset of symptoms, the greater will be the

chance of obtaining a good result—a fact which is not sufficiently stressed at the present time. The realization of this is a most important consideration in the treatment of gall-bladder disease, for early operation enables the disease to be attacked before widespread involvement of the biliary tract has taken place. Furthermore, in early removal of gall-stones lies the most certain method of preventing the complications to which they are so prone to give rise. Nevertheless, these cases still continue to appear before the surgeon after having been treated by palliative injections of morphia for many years.

It is true that disease of the biliary tract may be symptomless for a long period, so that it cannot always be possible to attack it in an early stage. Also, the degree of virulence of an infection may vary considerably, with the result that a virulent infection of a short duration may produce as much damage as, or even more than, one of a mild degree which has persisted some time. This may explain why, in certain cases of this series, following either drainage or removal of the gall-bladder, total relief of symptoms was obtained although these had been present for many years, and why, in other cases, only partial relief was obtained where the onset of symptoms preceded operation by only a few months. These considerations, however, do not outweigh the advisability of early operation.

A REVIEW OF OTHER REPORTED SERIES

A search through the literature shows that there have been seven series published recently of late results of operations on the biliary tract—namely, those of Bernhard,[1] Connell,[2] Davis,[3] Judd and Priestley,[6] Mason,[7] Sanders,[9] and Young.[11]

In Bernhard's series (1933), the operations were performed between 1900 and 1915, and in all 500 cases drainage of the common duct was combined with removal of the gall-bladder. He does not give the actual number of cases followed up, but states that of this number only 30 per cent are completely free from symptoms, a result which is extraordinarily poor. He next gives a list of the various recurrent symptoms in 180 cases and ascribes these complaints to two sources : (1) Inflammatory or other changes in the biliary tract; and (2) Changes in the gastrointestinal tract. Bernhard says that one can exclude the second group because these changes were also present before operation, and then he makes the strange statement that therefore 75 per cent are completely free from symptoms through operation. Secondary operations were undertaken in only 1·2 per cent of cases. He draws attention to the fact that one of the dangers of choledochostomy is a subsequent cicatricial stenosis, yet it is not mentioned as having occurred in any of the cases in his own series.

Connell (1928) reports on 99 surviving cases operated upon from 1910 to 1920. He found that in cases with stones, cholecystectomy gave better results than cholecystostomy, the respective percentages of cases without return of symptoms being 66·6 and 44·5. In non-calculous cases the corresponding figures were 75·0 and 77·3 per cent. There were 14 cases which came to secondary operation, the primary operation having been cholecystostomy in 13 and cholecystectomy in 1. It is of interest that in one of his cases, two years after cholecystostomy for calculous cholecystitis, a primary carcinoma of the gall-bladder was found. Secondary cholecystectomy was done in 7 cases, with relief in 4.

Davis (1928) follows up 144 cases of cholecystectomy, all done since 1921, so that

none of these has a post-operative history of more than seven years. Taking the series as a whole, 69·4 per cent were 'cured', but the results were definitely better in cases with stones (79·7 per cent cure in 69 cases) than in those without (60·0 per cent cure in 75 cases).

The most striking series is that reported from the Mayo Clinic by Judd and Priestley (1932). They deal with 606 satisfactory replies to questionnaires sent out to 1652 patients who were operated upon for disease of the biliary tract between 1907 and 1910, so that all have a post-operative history of more than twenty years. They found that cholecystectomy afforded results distinctly better than those following cholecystostomy in both calculous and non-calculous cases, the difference in 'satisfactory' results being about 24 per cent in favour of the former operation in each type of case, the average percentages being 84 and 60. No case of cholecystectomy came to secondary operation, while of those who had cholecystostomy performed, 17 per cent of calculous, and 12 per cent of non-calculous, cases were subjected to further operation. The predominant pathology found at these secondary operations was cholelithiasis, the calculi being found chiefly in the gall-bladder. Excepting that of Bernhard, this series is the only one in which results are mentioned in cases in which drainage of the common duct was employed. In calculous cases this procedure combined with cholecystostomy yielded satisfactory results in 76·8 per cent, and when performed alone or with cholecystectomy, 86·6 per cent gave a similar result. It was found that, following cholecystostomy, patients without stones had less subsequent trouble than those in whom stones were present, whereas after cholecystectomy the results seemed to bear no relationship to the presence or absence of stones. The results of an inquiry into the present state of health of 385 surviving cases suggest that the relation between disease of the gall-bladder or biliary tract and diseases of the joints or cardiovascular system seems quite definite, and the writers consider that the relatively large percentage of deaths in 65 cases which were due to cardiac disease and apoplexy confirms this association.

Mason (1931) has followed up 100 cases of chronic gall-bladder disease treated surgically by cholecystectomy five to fifteen years ago and another 100 which were given medical treatment during this period. He found that in the surgical cases 56·2 per cent stated that they were definitely relieved of all their old symptoms, and 83 per cent considered that operation had relieved 75 per cent or more of their previous complaint of pain. In contrast to these results, medical treatment completely relieved only 33 per cent, a similar percentage came to operation three to five years after the diagnosis of gall-bladder disease had been made, and the remaining third, because of the continuance of their symptoms, should have come to operation.

Sanders (1930) reports on 352 traced cases of cholecystectomy operated upon during the period 1921-8. He found that 84 per cent of these patients were completely relieved of symptoms and thinks that the removal of the appendix, carried out in the majority of these cases, may have favourably influenced the results, although Judd and Priestley found that appendicectomy made no difference. At the end of his article Sanders tabulates the results of 13 other series of cholecystectomies reported up to 1928. In 7 of these series the percentage of patients who are 'well' is between 80 and 90, in 4 it is between 60 and 70, in another over 90, and in the remaining one between 50 and 60.

Young (1928) reports results in 115 cases for a period ending 1925, this date therefore limiting the length of post-operative history of some of his cases to 3 years. Cholecystectomy was performed in all but 7 cases, in which cholecystostomy was done. He found that 63 per cent were 'cured', 22 per cent relieved of their main symptoms, and that 15 per cent were the same or worse. The 7 cases of cholecystostomy are all numbered amongst the cures, while all of those who have obtained no relief had their gall-bladders removed. The cystic gland was noted as being definitely enlarged in 13 cases, and as 8 of these belong to the group who were the same or worse after operation, Young thinks that such an enlargement suggests a focus of trouble elsewhere than in the gall-bladder.

A perusal of this review shows that several factors combine to render difficult, if not impossible, a satisfactory comparison of results. The same classification is not always used; the length of the periods of post-operative observation and the number of cases whose results are investigated are subject to considerable variation, and in some reports the degree of detail leaves much to be desired. However, one gets the impression that, on the whole, cholecystectomy gives definitely better results than cholecystostomy, both in regard to the actual percentage of cases benefited by operation and the possibility of the necessity of secondary operation.

CHOLECYSTOGRAPHIC   STUDIES

The amount of restoration of function that may take place in a diseased gall-bladder which has been drained is of great importance when considering the comparative value of cholecystostomy and cholecystectomy. The belief that little or no restoration of function takes place materially strengthens the claim for removal of the diseased gall-bladder as the treatment of choice except under conditions such as would render the more difficult operation of cholecystectomy an unjustifiable risk. It was in the hope of being able to confirm or refute this belief that this radiological investigation was undertaken. It was made possible through the co-operation of Dr. Whately Davidson, Honorary Radiologist to the Royal Victoria Infirmary, Newcastle-upon-Tyne, and to him and his technical staff my thanks are due.

At present the only means at our disposal of determining the function of the gall-bladder is by cholecystography, the method associated with the names of Graham and Cole, and one which, though subject to limitations, gives reliable information in a high percentage of cases. Since the general consensus of opinion and experience now is that intravenous administration of the dye yields no better results than when it is given by mouth, it was decided to administer the dye by the latter route, and a dose of 4 grm. of tetraiodophenolphthalein was given in each case. I am indebted to Mr. Foggin, Head Pharmacist to the Royal Victoria Infirmary, for his preparation of the dye in the form of a palatable beverage.

The following was the routine carried out. The patient was instructed to have the bowels thoroughly evacuated the day before the administration of the dye, which was taken, after the usual supper, at 9.0 p.m. just before retiring X-ray photographs of the gall-bladder were taken the following day at 9.0 a.m. and 3.0 p.m., i.e., twelve and eighteen hours after the ingestion of the dye. No food was allowed after taking the dye until the completion of the examination,

but no restriction was placed on the drinking of water during this time. A fatty meal was not given in the interval between the photographs, the routine in this respect following that advised by L. A. Rowden,[8] of Leeds, who, from his extensive experience, has found that if the gall-bladder fills and concentrates well, it also empties well. In consequence, he considers the giving of a fatty meal unnecessary.

Prior to submitting the patients to cholecystography, the writer himself underwent the examination in order to furnish a normal control for purposes of comparison. A very satisfactory result was obtained as can be seen from *Fig.* 206 ;
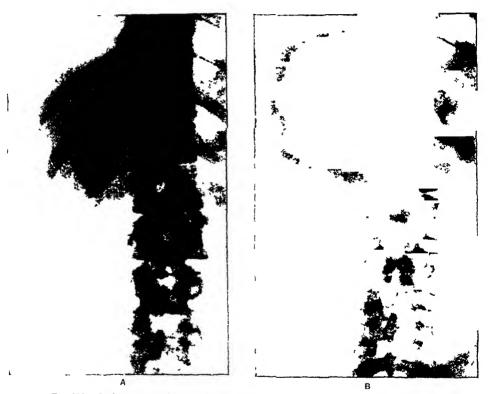
FIG 206 —Cholecystogram of author for purposes of normal control   A (twelfth-hour film) shows the shadow of the gall-bladder to be of good and even density   B (eighteenth-hour film) shows an increase in both size and density of the shadow

at the twelfth hour the shadow of the gall-bladder was of good and even density, and at the eighteenth it was slightly larger and the density had definitely increased, showing that the gall-bladder had both filled and concentrated well.

Arrangements were made for 50 patients of this series, all of whom had had cholecystostomy performed during the period 1907–22, to attend the Radiological Department as out-patients during the latter part of 1933. On completion of the cholecystograms it was found that only 24 patients had attended ; of these, 6 had not taken the dye and therefore must be disregarded. This leaves 18 cases for consideration : the earliest cholecystostomy was done in 1911 and the latest in 1922, so that an interval of eleven to twenty-two years had elapsed since operation ;

stones were found in every case at operation; in 14 cases the accompanying cholecystitis was chronic, and in 4 acute.

In brief, the results obtained were as follows. In 7 cases (38·9 per cent) the shadows were of good density on the first film and the density increased to such a degree on the second as to indicate that the gall-bladder was filling and concentrating well, these findings being interpreted as showing that the function of the organ was good; *Fig. 207* shows a cholecystogram representative of those obtained in this group of cases. In 9 cases (50·0 per cent) the shadows were faint on the first film and little or no increase in density was shown on the second, these

A   B

FIG. 207.—Cholecystogram. K. D. Cholecystostomy, 1922. Taken as representative of the seven gall-bladders with good function. Good shadow of gall-bladder in A (twelfth-hour film), with increased size and density in B (eighteenth-hour film).

findings indicating that the gall-bladder function was definitely impaired. In the remaining 2 cases (11·1 per cent) the gall-bladder was not visualized at all and so was considered to be a functionless organ.

The relationship between the function of the gall-bladder on the one hand and the clinical results and type of cholecystitis present at operation on the other are given in *Tables XV* and *XVI*.

It is of interest that both patients in whom the gall-bladder is a functionless organ belong to the group who have obtained total relief of symptoms following operation. One explanation of this seems to lie in the complete, or nearly complete, destruction of the mucous membrane by the inflammatory process which affected the gall-bladder. In this way the organ would be deprived of its power of absorption and so be unable to concentrate the dye. Moreover, in such cases the gall-bladder usually becomes a shrivelled-up mass of fibrous tissue with little or no lumen. If a small amount of secreting epithelium still survives, and if the

cystic duct still remains patent so as to allow the escape of the secretion into the common duct, then no symptoms are likely to arise from such a gall-bladder *per se*. The pathological picture, therefore, is that of a natural cure. A second explanation which might be offered also concerns a form of natural cure—namely, mucocele, due to complete obstruction of the cystic duct by such causes as calculus or stricture with resulting paresis of the gall-bladder wall. In such a condition the gall-bladder would also not be visualized by cholecystography owing to the

Table XV.—CLINICAL AND CHOLECYSTOGRAPHIC RESULTS IN 18 PATIENTS AFTER CHOLECYSTOSTOMY

CLINICAL RESULT	GALL-BLADDER FUNCTION		
	Good	Impaired	None
Total relief..	4	4	2
Partial relief	2	–	–
No relief ..	1	5	–

Table XVI.—CHOLECYSTOGRAPHIC RESULTS IN 18 PATIENTS AFTER CHOLECYSTOSTOMY FOR ACUTE AND CHRONIC CHOLECYSTITIS

TYPE OF CHOLECYSTITIS	GALL-BLADDER FUNCTION		
	Good	Impaired	None
Acute ..	2	1	1
Chronic ..	5	8	1

dye-laden bile being prevented from entering the organ. However, the forcible contractions of the unstriped muscle of the gall-bladder wall which precede the subsequent paresis in such a case would probably have given rise to an attack of biliary colic. Furthermore, a mucocele of the gall-bladder has a tendency to become infected sooner or later, with recurrence of symptoms. Thus, of these two explanations, the former remains the more probable.

The presence of a normally-functioning gall-bladder after cholecystostomy in patients in whom there is a recurrence of apparent biliary symptoms is of importance as it suggests they may be due to causes other than disease of the gall-bladder and indicates the advisability of an investigation of other systems.

The percentage of cases showing normal function of the gall-bladder following cholecystostomy for acute cholecystitis is somewhat greater than that following this operation for chronic cholecystitis. While these results point in an expected direction, yet the number of cases is too small to permit of conclusions being drawn from them.

In these cholecystographic studies the length of time which had elapsed since operation was not found to bear any relation to the present degree of function of the gall-bladder.

While the present degree of function of the gall-bladder in each of these 18 cases, as shown by the cholecystogram, is known, a comparison of this with the pre-operative function is not possible, for cholecystography had not been introduced when the operations took place. While, therefore, the actual amount of restoration of function which may have taken place must remain unknown, one important fact is brought to light by the results obtained in this investigation. It is that in 11·1 per cent of the cases the gall-bladder is now functionless and in another 50 per cent the function is now definitely impaired. Thus, in the majority of cases, cholecystostomy has failed to restore the function of the gall-bladder to normal.

With regard to the 38·9 per cent of patients whose gall-bladders have now a normal function according to the cholecystograms, it must be borne in mind that one or more of these gall-bladders might have shown a normal response to the dye before operation, for cholecystography has taught us that such a result may be obtained if only a mild degree of inflammation of the gall-bladder is present. To assume that the function of the gall-bladder in the cases of this group was definitely impaired before operation and has thus been restored to normal by operation makes the present percentage of such cases much higher than that for similar ones reported by the authors quoted below. Even granting this assumption to be correct, there are still good reasons why this comparatively high percentage should not be regarded as an argument in favour of cholecystostomy. In the first place, it represents the minority of cases, and, secondly, we have not yet the means at our disposal of knowing which infected gall-bladder will have its function restored to normal by cholecystostomy and which will not.

It is interesting to make a comparison of these results with those of other reported series of cholecystograms following cholecystostomy. Spurling and Whittaker[10] carried out cholecystography, giving the dye intravenously, on 12 patients in whom an interval of twenty-five days to nineteen years had elapsed since operation. They found that the gall-bladder was visualized in every case, but none showed a normal shadow, so that all these patients had gall-bladders the function of which was impaired. In 4 cases the cholecystogram showed the presence of stones in the gall-bladder, and these findings were verified at subsequent secondary operation. In another 2 patients who came to secondary operation, the gall-bladder was found to be markedly thickened and sclerotic. These authors came to the conclusion that drainage of a diseased gall-bladder with the expectation that it will regain its normal function is not only a futile procedure but one that endangers the future health of the patient. Fleming[5] investigated the function of the gall-bladder by oral cholecystography in 36 patients whose average time since cholecystostomy was three years and ten months, the longest time being ten years and the shortest six months. He found a normal response to the dye in only 1 case, and in the large number of 29 the gall-bladder was not visualized at all, leaving 6 in which visualization occurred but was impaired. Thus his study indicated that the function of the gall-bladder was entirely lost in 80 per cent and impaired in 17·3 per cent of the remaining 20 per cent. Fourteen of the 29 cases whose gall-bladders were not visualized by the dye had been free from symptoms since their operation; the single normal response was found in a patient whose health had improved since operation though complete freedom from symptoms had not been obtained. Eliason and Ferguson[4]

undertook a cholecystographic study of 28 patients one or more years after chole-cystostomy, the dye being given by mouth. In only 1 of 20 patients whose operative findings showed evident cholecystitis did the cholecystogram indicate a normally-functioning gall-bladder. In 8 of the patients studied the gall-bladder at operation appeared normal; 5 of these (3 non-calculous and 2 calculous) showed a normally-functioning gall-bladder, while in the remaining 3 (calculous), impaired function was noted. Their results lead these authors to the conclusion that cholecystostomy *per se* does not greatly alter the function of the gall-bladder.

SUMMARY AND CONCLUSIONS

1. An investigation was undertaken of the late results of operations on the biliary tract which were performed between the years of 1907 and 1922. Attempts were made to follow up 790 patients and were successful in 359, of whom 305 still survive.

2. The difficulties encountered in the interpretation and classification of the results are mentioned and discussed.

3. In both acute and chronic cholecystitis with cholelithiasis, cholecystectomy was followed by better results than cholecystostomy; the percentage of patients who obtained relief, both total and partial, being greater in patients in whom the gall-bladder was removed. Hence it is considered that cholecystectomy is to be preferred to cholecystostomy unless contra-indications to its performance exist.

4. Attention is drawn to the excellence of the results in cases with and without choledochlithiasis in which drainage of the common duct was combined with cholecystostomy or cholecystectomy. It is considered that an important factor in the production of these results is the additional drainage of the common duct. Thus a plea is made for the more frequent opening and exploration of the common duct in cases where the gall-bladder is the seat of marked inflammatory change, especially of the chronic type; it is the most certain way of ascertaining the presence of stones in this portion of the biliary tract and the exploration can be followed by drainage, thereby acknowledging the widespread nature of infection of this tract and applying the principle of treatment governing its eradication.

5. Several cases are reported which, after drainage or removal of the gall-bladder, had one or two or even three recurrent attacks over a long period of time, each attack subsiding and leaving the patient perfectly well. It is suggested that these attacks are due to a transient inflammation of the biliary tract. It is felt that wide recognition should be given to the existence of such cases in order that unnecessary secondary operations may be avoided.

6. In all the patients who claim to have obtained no relief from operation, recurrence of symptoms took place within a period of three years after operation, and, in the majority, before one year had elapsed. This seems to indicate that the earlier the recurrence of symptoms after operation, the more likely they are to persist.

7. An analysis of the causes of death which occurred in 43 cases of this series after leaving hospital shows that carcinoma and cardiovascular disease were responsible for the greater number. The fact that carcinoma of the gall-bladder did not occur in those patients who had cholecystostomy performed suggests that the drained gall-bladder is no more susceptible to carcinoma than one which has not been subjected to that procedure. Reasons are given why it is not deemed

justifiable to conclude that the deaths from cardiac disease were the result of a systemic infection due to the drained gall-bladder persisting as a focus of infection.

8. The percentage of patients who came to secondary operation after cholecystostomy was five times greater than that following cholecystectomy. The predominant pathology found at the secondary operations was cholelithiasis, characterized mostly by the re-formation of stones in the gall-bladder. In cases where primary cholecystostomy had been performed, secondary cholecystectomy has given much better results than secondary cholecystostomy. The increased liability to secondary operation which attends cholecystostomy and the possibility of the gall-bladder persisting as a focus of infection after this operation emphasize the importance of primary cholecystectomy as the operation of choice. The success of secondary cholecystectomy indicates that it is the best line of treatment to be adopted in these cases.

9. In so many patients a recurrence of symptoms did not take place until five or ten years following operation that figures for five- and ten-year results were compiled. The ten-year results are so much better than those representing the series up to twenty-five years after operation, and the five-year results correspondingly better than the ten-year, as to prove that results published after a relatively short period of post-operative observation should not be accepted as truly representative of the efficacy of operation.

10. A consideration of the length of pre-operative history of the cases in this series offers confirmatory evidence of an aspect of biliary tract disease which is not sufficiently stressed at the present time—namely, that the earlier operation is performed, the greater will be its chance of success.

11. Cholecystographic studies were made of 18 patients who had had cholecystostomy performed eleven to twenty-two years ago. In 61 per cent of cases the function of the gall-bladder is impaired or lost, indicating the failure of cholecystostomy to restore this to normal in the majority of cases. This is a further argument in favour of cholecystectomy as the treatment of choice of the pathological gall-bladder.

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TRAUMATIC RUPTURE OF THE CONGENITAL SOLITARY KIDNEY

By J. R. H. TURTON

SURGEON, ROYAL SUSSEX COUNTY HOSPITAL, BRIGHTON

AND J. C. F. LLOYD WILLIAMSON

SURGICAL REGISTRAR, ROYAL SUSSEX COUNTY HOSPITAL, BRIGHTON

CONGENITAL absence of one kidney is uncommon, but Eisendrath[2] has shown that it is not of extreme rarity. He found in his series that it occurred in 0·1 per cent of autopsies, and he was able to trace the records of forty cases. Males predominated. The solitary kidney was more commonly on the right (in our series every case was left), and was usually, but not invariably, in the normal position : it was found to be hypertrophied, sometimes to double the normal size.

A true unilateral kidney is usually associated with a single unilateral ureter and a single opening into the bladder, but in 7 per cent of cases some trace of the opposite ureter may be found (Thomson-Walker[7]). There may be no trace of the ureteral orifice, or this may be marked by the presence of a small dimple, but in some cases an orifice has been found to be present opening into the lumen, which extends for 1 or 2 cm. along the fibrous cord which represents the ureter. This half of the trigone of the bladder may be atrophied.

The frequency of the absence of the suprarenal gland on the side of the missing kidney appears to vary considerably in different series. Eisendrath[2] records 10 to 25 per cent in various reports ; Thomson-Walker[7] states that it is absent in 27·7 per cent of cases. The renal vessels are usually absent or quite rudimentary. The condition may be associated with genital abnormalities (Eisendrath[2] and Brattström[1]).

A number of cases have been reported in which nephrectomy has been performed on account of a neoplasm or disease of a kidney, which proved later— at post-mortem examination—to be of the congenital solitary type. In contradistinction to this a thorough search of the literature has disclosed but four reported cases of traumatic rupture of the congenital solitary kidney. An analysis of these cases is shown in *Table I*, and to these is now added a fifth.

CASE REPORT

HISTORY.—S. D., a schoolboy aged 12, on the morning of Oct. 29, 1932, fell off a gate about 5 ft. high on to his left flank. He was taken home and put to bed. He complained of pain in the left loin, vomited several times, and passed blood in the urine. Later he was seen by his doctor, who found that his abdomen was rigid on the left side, and sent him up to the Royal Sussex County Hospital for admission.

ON ADMISSION (9.45 p.m.).—Intelligent boy ; pale ; no air-hunger. Temperature 96·8°, pulse 100, respirations 20. Abdomen moved slightly, but this and coughing were painful. No sign of shifting dullness. The percussion note was impaired, increasing to absolute dullness in the flank (*Fig.* 208). Urine : small specimen, almost pure blood.

*Table I.—*Analysis of Cases of Traumatic Rupture of Congenital Solitary Kidney

Author and Date	Sex and Age	Occupation	Side of Kidney	Nature of Accident	Nature and Time of Operation	Day of Death (after Accident)	Notes
1. Melchior[1] (Germany) 1928	M. 27	Doctor	L.	Motor accident	1. Laparotomy. 2. Nephrectomy. Day after accident	5th	On admission general condition good. Bruising in L. flank. Bladder contained pure blood; next day worse. Anterior laparotomy showed some distension, but no intraperitoneal injury. Hæmorrhage round L. kidney. Wound closed. Lumbar nephrectomy. Kidney showed deep transverse cut into hilum
2. Speer[5] (U.S.A.) 1929	M. 27	'An Italian'	L.	Motor accident	Nephrectomy soon after admission	Soon after 1st day	Conscious on admission. Also fracture of L. femur. Very shocked, but improved a little, so operation. Kidney showed complete tear into pelvis and vein
3. Brattström[1] (Sweden) 1932	F. 16	Schoolgirl	L.	Kicked by horse while bicycling	Nephrectomy soon after admission	3rd	On admission bladder full of pure blood. Condition rapidly deteriorated, so operation performed. Kidney found to be pulped. At post-mortem examination no ureter or suprarenal present, and uterus bifid
4. Thompson[6] (Ireland) 1932	M. 22	?	L.	Kicked in L. loin at football	Nephrectomy several days after accident	10th after operation	This patient was watched for some days, first at home and then in hospital before the persistence of pain and bleeding demanded operation. L. kidney showed deep cut into pelvis and was 'hopelessly' damaged
5. Turton and Williamson (England) 1932	M. 12	Schoolboy	L.	Fell about 5 ft. off gate on to L. flank	Drainage of retroperitoneal extravasation 11th day after accident	11th	Expectant treatment at first and patient improved, but then became worse. (*See* case report and photograph of kidney)

COURSE.—

Oct. 30–Nov. 6.—The condition improved gradually. The patient began to feel and look better, although he was still very ill. He complained of pain, severe at times, in the left flank. The area of impaired percussion note started to recede into the flank. The urine increased in amount, and became less blood-stained. (The output on Nov. 2nd and 5th was 43 and 30 oz. respectively.)

Nov. 6–9.—After becoming clear the urinary output lessened and soon stopped. A catheter showed the bladder to be empty. The general condition became worse. He complained of pain, suprapubic, and in the left iliac fossa and left loin, and there was an ill-defined tender swelling in these regions. He became drowsy.

A diagnosis was made of an infected extravasation of urine and blood, around and below the ruptured left kidney —producing anuria—and a simple drainage operation was decided on.

FIG. 208.—Diagram showing area of diminished percussion note in case of ruptured solitary kidney.

OPERATION (Nov. 9).—Under a general anæsthetic a left gridiron incision was made near the anterior superior iliac spine. A large amount of urine (proved chemically later), and some clots were rapidly evacuated from the extraperitoneal tissues below the left kidney. A drainage tube was inserted and another through a stab-wound in the left loin. As this was finishing the heart and respiration stopped. Although these were restarted, after thirty minutes they stopped again—finally.

POST-MORTEM EXAMINATION (by Dr. L. R. Janes).—

Left Kidney.—Rupture extending from the capsule to the pelvis at the lower pole. Much perinephric extravasation of blood, with some retroperitoneal extravasation extending to the opposite side of the abdomen, and down into the pelvis with commencing organization.

Right Kidney.—Absent together with ureter.

Right Suprarenal.—No trace found.

Bladder.—Right ureteral orifice absent, left natural. Right side of trigone atrophic (*Fig.* 209). Some small ecchymoses on the subperitoneal surface of the bowel and bladder (patchy in distribution and independent of retroperitoneal extravasation). No hæmoperitoneum. Operation drains in good position for drainage of lower pole of kidney. Much bruising of perineal and scrotal region. No scar of any previous operation seen (such as nephrectomy).

Spleen, Liver, and Thorax.—No injuries.

FIG. 209.—Post-mortem appearances of left kidney and ureter, and of bladder. A, Lower pole of left kidney showing extensive laceration, B, Atrophic right side of bladder; C, Internal urethral orifice, D, Probe in left ureteral orifice (note this lies between two areas of submucous hæmorrhage), E, Left ureter.

COMMENTARY

In *Case* 5 the diagnosis was up to a point correctly made—rupture of the left kidney—and the patient was watched and treated as such. As his condition improved it was thought that the rupture was not sufficiently severe to need immediate or early operation. The possibility of the absence of the right

kidney was never considered, nor was nephrectomy proposed when operation became imperative.

Three questions arise : (1) Whether an attempt should be made in every case of kidney injury to determine the presence or otherwise of a functioning second kidney. (2) If this is considered desirable, is it possible, and what means are available ? (3) If the damaged kidney is proved to be the only functioning organ, what is the most appropriate line of treatment ?

1. Although a search of the literature has discovered only five cases (including that now reported) of rupture of a single kidney, the incidence of congenital single kidney as shown in Eisendrath's[2] statistics is not so rare as to render it probable that these are the only cases in which rupture of a solitary kidney has occurred. It would appear likely that many less severe, and therefore non-fatal, cases of rupture of a solitary kidney have gone unreported, and in all probability the unilaterality was not suspected. It would therefore seem desirable that the presence of a functioning kidney on the other side should be proved or disproved.
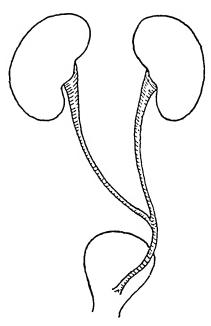
FIG. 210.—Diagram of Hepburn's case, in which the two ureters united to end in a single ureteral orifice. (*After Eisendrath.*)

2. The possible means of ascertaining the presence of a second functioning kidney:—

a. *Cystoscopy* in these cases is usually very difficult owing to hæmorrhage continually obscuring the view of the ureteral orifices (Melchior[4]). Moreover, even if a clear view is obtained and hemiatrophy of the trigone and absence of one orifice is proved, the case might be one of rupture of one kidney in a patient, such as the one described by Hepburn[3], in which there was a single ureteral orifice normally located but two kidneys, the ureters from these having united before entering the bladder (*Fig. 210*). Cystoscopy, therefore, even if possible, is of little practical value in any case, whatever its degree of severity, and moreover is scarcely justifiable owing to the very definite risk of conveying infection (Thomson-Walker[7]).

b. *Intravenous pyelography* does not appear to have been done in any of these cases, but at any rate in the less urgent cases it would seem to offer the only pre-operative means of determining the presence of a second functioning kidney. There would not seem to be any contra-indication to its employment in such a case.

c. Unless it has been possible by intravenous pyelography to prove the presence of a functioning contralateral kidney, the peritoneum must be opened and *palpation of the opposite renal fossa* (and if empty, below this, in case the other kidney is ectopic) can and should be done before nephrectomy. This method is available in the most urgent type of case, especially in those very severe ones in which anterior laparotomy is performed owing to the possible injury to other viscera.

3. The answer to this question is sufficiently obvious. If the only kidney is damaged, every effort should be made to arrest hæmorrhage by conservative suturing or partial nephrectomy.

CONCLUSIONS

1. A case of rupture of a congenital solitary kidney is quoted and four other cases are tabulated.

2. Rupture of congenital solitary kidney is distinctly rare.

3. It occurs most commonly in men, usually on the left side and in young patients, the figures in this series being : Males to females, 4 to 1 ; left to right, 5 to 0 ; average age, 21 years.

4. Unless the rupture is slight, when the diagnosis of a congenital solitary kidney has not been made, the condition has not been suspected, and has only been found post mortem.

5. In any case of renal injury, where nephrectomy is contemplated : (a) Where the condition of the patient permits, intravenous pyelography should be employed as a means of demonstrating the presence of a second functioning kidney ; (b) In the severe type manual palpation for the contralateral kidney must be employed at operation.

6. If the rupture is proved to be that of a solitary kidney, the operative measures adopted must be conservative.

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SQUAMOUS-CELL CARCINOMA OF THE RENAL PELVIS: REPORT OF A CASE

BY MAURICE SILVERSTONE

HONORARY ASSISTANT SURGEON, BIRKENHEAD GENERAL HOSPITAL

TUMOURS of the renal pelvis form 5 to 7 per cent of all renal tumours,[1] and these in turn form $\frac{1}{2}$ to 2 per cent of all tumours, occurring in about 1 in every 400 patients.[2]

Ewing[3] has divided these tumours into: (1) Benign papilloma; (2) Papillary epithelioma; and (3) Flat or alveolar carcinoma. The last group would include the squamous epithelioma type, but amongst the group would also be included the advanced cases of papillary epithelioma where the papillæ had become so flattened and compressed together as to render their original papillary formation indistinguishable.

Kretschmer[4] collected 43 cases of non-papillary carcinoma, of which 17 were thought to be epidermoid. Since then cases have been published by, amongst others, Wells[5] (1 case), Scholl and Foulds[6] (5 cases between 1907 and 1922 at the Mayo Clinic), and 1 case each by Keynes,[7] Wheeler,[8] Herman and Greene,[9] and Bowen and Bennett.[10] Jocelyn Swan,[11] in a personal series of 65 cases of new growths of the kidney, had 2 cases of papillary carcinoma, 2 of squamous epithelioma, and 1 of benign papilloma. Cabot and Allen[12] collected 27 cases of malignant renal pelvic tumours at the Mayo Clinic between 1923 and 1932, of which 24 were papillary, 2 non-papillary, and 1 was a mixed papillary and sessile tumour. Swift Joly,[13] in a collected series of 337 cases of renal pelvic tumours, found 120 cases of benign papilloma, 138 cases of papillary carcinoma, 29 cases of transitional-cell carcinoma, and 50 cases of squamous-cell carcinoma.

In view of the comparative rarity of non-papillary carcinoma (squamous epithelioma) of the renal pelvis, it was thought of interest to put on record an additional case, especially since it was unassociated with the presence of any stone or gross renal infection.

CASE REPORT

HISTORY.—The patient, a married man of 54, by occupation a coppersmith, was admitted to hospital with the history of having been perfectly fit, apart from an attack of malaria sixteen years previously, till three months before. At this time he had some vague pain in the lower part of his back on both sides. This he treated himself, and it passed off after about a week. About a month later he started with renal colic on the right side; at first the pain was ill-defined, but after a day or two it became severe. Associated with the pain he had hæmaturia, slight frequency which he attributed to an increased fluid intake, and some strangury. The condition improved after a few days. Six weeks later and just prior to his admission he again passed blood with his urine. On this occasion the pain was in the lower abdomen and equally severe on the two sides. There was no definite colic. He said he had lost over two stone in weight during the past three months.

ON EXAMINATION.—The patient had obviously lost weight. The right kidney was palpable and felt rather hard, but moved normally on respiration. There were no signs of disease elsewhere.

Microscopic examination of his urine revealed the presence of some blood, occasional pus cells, and many *B. coli* The non-protein nitrogen of the blood was 37 mgrm. per cent.

A cystoscopy was carried out. The ureteric orifices were normal, blood was coming out of the right. Indigo-carmine excretion test showed dye appearing from the left orifice in six minutes and from the right in ten minutes. A pyelogram on the right side showed the lowermost calix attenuated and deviated to one side, the remainder of the pelvis appearing normal. Uroselectan examination showed a possibly slight hydronephrosis on the *left* side, whilst on the right the lower calix was not seen, the remainder of the kidney apparently excreting normally.

DIAGNOSIS.—A diagnosis of malignant disease of the kidney was made and operation decided on.

OPERATION. The kidney was explored through a right renal incision. It was only very slightly if at all bigger than normal, and adherent at the lower pole. A number of firm smooth glands extended from the pedicle upwards to the region of the liver. The lower pole was separated and the kidney removed, though it was really inoperable in view of the glands.

Convalescence was uneventful, the patient feeling much better after the operation, but at the time of discharge three weeks later he was beginning to go down hill, and he died two months after the operation.

EXAMINATION OF SPECIMEN.—The kidney was seen to be replaced at the lower pole, where it had been adherent, by a greyish-white tumour nodular at one point. On section the tumour was seen to involve the lower part of the pelvis and lower calix and to be

FIG 211.—Macroscopic appearance of tumour. (×⅓)

spreading into the substance of the kidney, involving rather less than its lower half. At the periphery of the growth were separate scattered foci in the substance of the kidney (*Fig.* 211).
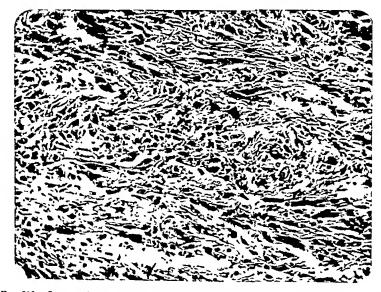
FIG. 212 —Section of tumour showing mixed- and spindle-celled type of growth. (× 190)

Microscopical examination of the growth was interesting. A section taken from the growing edge showed cells resembling those in a spindle- or mixed-celled sarcoma in part,
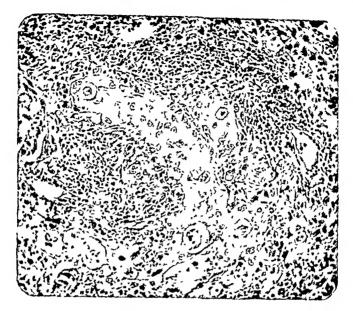
FIG. 213 —Section showing typical carcinomatous area. (×135.)
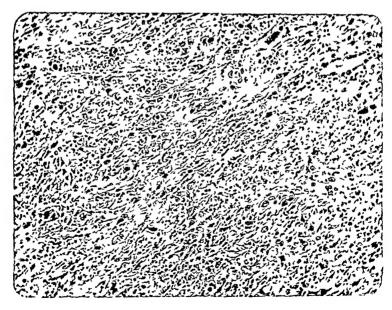
FIG. 214.—Gradation between *Fig.* 212 and *Fig.* 213. (×135.)

whilst the arrangement elsewhere was reminiscent of a carcinoma (*Fig.* 212). Further sections were therefore cut and these showed the tumour to be a highly malignant anaplastic carcinoma arising from the pelvis. No cell nests were seen (*Fig.* 213). A further section

(*Fig.* 214) shows the gradation between the typical carcinoma (*Fig.* 213) and the anaplastic sarcoma-like area (*Fig.* 212). There was no history of stone, and none was found, nor was there any gross infection of the kidney.

DISCUSSION

Etiology.—The condition is twice as common in males as in females, and 50 per cent of the cases occur between the ages of 40 and 60.[14]

As elsewhere in the urinary tract, squamous epithelioma arises from epithelium that has undergone metaplasia due either to infection, prolonged or of short duration but acute, or to chronic irritation, usually from stone. Of the cases collected by Kretschmer[4] 11 were associated with stone, 4 of the 5 cases reported by Scholl and Foulds[6] were associated with stone, as were the cases reported by Wells,[5] Keynes,[7] Wheeler,[8] and Bowen and Bennett.[10] Jocelyn Swan[11] in his series had one case with stones and one without. The cases collected by Cabot and Allen[12] were unassociated with stone, as was the case reported by Herman and Greene,[9] where the growth obstructed the pelvis of the kidney, producing marked hydronephrosis. Graham Simpson[15] mentions the possibility of one of his cases having been a non-papillary carcinoma arising from the renal pelvis, and this was unassociated with stone.

Herman and Greene suggest that the tumour may arise from developmental inclusions of ectodermal cells, but feel that chronic irritation or infection is the usual predisposing factor. Pascual,[16] however, considers infection not to be important etiologically, as he would have expected tuberculous disease of the kidney to be more commonly associated with carcinoma.

Pathology.—There are two types of tumour. In one, of which the case reported is an example, the renal parenchyma is invaded early, the kidney being replaced by carcinoma. As the growth passes to the periphery the epithelium becomes more anaplastic, more rapidly growing and primitive, so as to resemble a carcinoma simplex. This is commonly associated with stone. In the second type the renal pelvis is covered by numerous tumour masses some of which may be papillary: the pelvi-ureteric junction is obstructed by growth so that the kidney, which is not invaded, and the pelvis become hydronephrotic, and the kidney tissue atrophies.

The case described by Keynes[7] is of interest. There a calculous pyonephrotic kidney was removed and the patient returned with recurrence of swelling three months later. It was noticed that there was some granulation tissue at the site of the scar, and a section of this showed cells resembling those of a round- or spindle-celled sarcoma. Re-examination of the removed kidney showed a plaque which microscopically proved to be squamous epithelioma. In the case reported the anaplastic carcinoma at the growing edge of the growth resembled a spindle-celled sarcoma. The case described by Keynes is the only one that could be found to have a similar type of cell, though in his case it was in a recurrence.

Metastases.—In both types these are early and widespread. They invade the local lymphatic glands extending to the liver. Metastases also take place by the blood-stream and are found in the liver, lungs, and bones. In non-papillary carcinoma there is no tendency for implantation to occur lower down in the urinary tract.

Clinical Course.—The cases associated with stone usually have a long history, that of stone, and then perhaps an increase in the severity of the symptoms may make one suspect the onset of neoplasia. Hæmaturia in the non-papillary type occurs in about half the cases.[9] The relative infrequency of this symptom is probably due to the fact that the tumour does not tend to ulcerate deeply and in a certain proportion of cases obstruction takes place at the pelvi-ureteric junction. In the majority of published cases there has been a marked loss of weight; the patient reported lost two stone in three months. The kidney may be palpable and may be much enlarged; in the latter case this is often a result of the preceding infection or calculous disease.

Although diagnosis of the exact microscopical lesion is difficult, the association of hæmaturia with marked loss of weight should make one suspect malignant disease. Unfortunately in a proportion of cases attention is not drawn to the kidney until the condition is inoperable.

Prognosis.—This is bad. Of eight cases of squamous-celled carcinoma on whom nephrectomy was performed reported by Kretschmer, five died soon after the operation and the remainder developed metastases early. Of the cases collected by Scholl and Foulds, one died eleven days after the operation, two two months after, and one, which was partly papillary and partly sessile, died four and a half years later. Of the three cases reported by Cabot and Allen, one lived eight months and died from stomach trouble, one died within ten days and had metastases in the liver, and one was reported well two months after the operation. The diagnosis of non-papillary or squamous-celled carcinoma of the renal pelvis carries with it a hopeless prognosis, the average duration of life being between ten and eleven months, though that in the papillary type of growth would appear to be more favourable, thirty-seven months (Cabot and Allen[12]).

I am indebted to Professor T. B. Davie and Dr. Hugh Smith for the microscopical report on the tumour.

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SACRO-COCCYGEAL   CYSTS   AND   TUMOURS

By RONALD W. RAVEN, London

ASSISTANT SURGEON TO GORDON HOSPITAL FOR DISEASES OF RECTUM, LONDON

THE sacro-coccygeal region is one of the commonest sites in the body for the occurrence of anomalous cysts, sinuses, and tumours of various kinds. This is not surprising when the complex nature of the development of this part of the body is taken into account. Reference is made to the changes occurring in the caudal extremity of the primitive streak, to the formation and disappearance of the neurenteric canal and the post-anal gut, and to the formation of the terminal part of the intestinal tube by the development of the anal canal. Complicated changes also occur in connection with the genito-urinary system. It is possible that any of these primitive structures may leave a relic of their existence and furnish a contribution to that which has been described as a histological potpourri.

EMBRYOLOGICAL FEATURES OF THE SACRO-COCCYGEAL REGION

In the early stages of development the caudal end of the body is the site of very rapid and complex changes. The primary tissue of the entire digestive system is entoderm, and this forms a tube which extends first into the head region as the fore-gut and later caudally as the hind-gut (*Fig.* 215). The fore-gut becomes the mouth, pharynx, and a portion of the small intestine. The hind-gut forms the colon, rectum, and part of the small intestine. The region between these two extremities is the mid-gut, which opens ventrally into the yolk sec. At each extremity the entoderm gut comes into direct relationship with the ectoderm, and fusion occurs between these two layers with the formation of the oral and cloacal membranes. The hind-gut forms a subterminal dilatation which is bounded on the dorsal aspect by the aorta and notochord and ventrally by the ectoderm of the body wall. It is on the ventral wall of the cloaca that the cloacal membrane is formed (*Fig.* 216). The hind-gut and allantois open into the anterior wall of the cloaca ; the mesonephric ducts open into the dorso-lateral
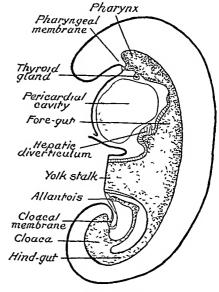
FIG 215 —Extent and relations of the primitive entodermal tract shown by stereograms of the right half of human embryos at 2 5 mm. (ˣ 30) (*After Thompson — from Arey's 'Developmental Anatomy'.*)

walls and the post-anal gut into the posterior wall. The cloacal membrane extends from the umbilicus to the base of the tail, and thus is of considerable length but is narrow from side to side. The primitive entodermal gut extends
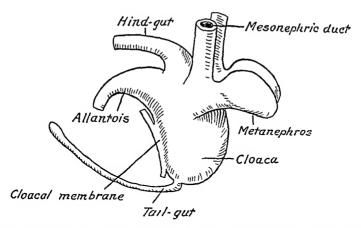
FIG 216 —Reconstructions of the human cloaca, viewed from the left side, during the earlier period of its division at 5 mm (40) (*After Pohlman—from Arey's 'Developmental Anatomy'*)

for some distance beyond the cloacal membrane and this portion is called the post-anal gut.

In embryos of 5 mm. the cloaca commences to divide into two portions by the development of the urorectal septum, which grows forward from a point between
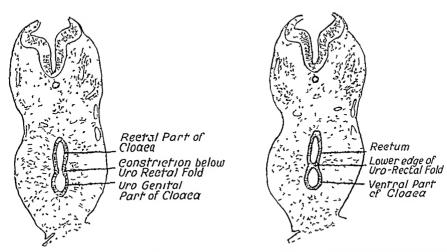
FIG. 217.—Transverse section through cloacal region of human embryo of 9 mm (× 35)

FIG 218 —Subdivision of cloaca into rectum and urogenital portion in human embryo of 9 mm (× 35)

the openings of the hind-gut and allantois until it meets the cloacal membrane, which is bisected into the urogenital and anal membranes (*Figs.* 217, 218). At a stage between 13 and 18 mm. both of these membranes are perforated and the intervening tissue differentiates into the perineum. The end of the hind-gut

(*Figs.* 219, 220) becomes lined with ectoderm for a short distance and this portion constitutes the anal canal. Wood-Jones has pointed out that the recto-vesical
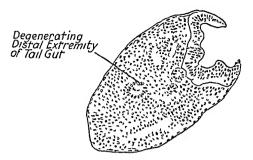
FIG. 219 —Transverse section through the tail end of a human embryo of 9 mm. (× 75)
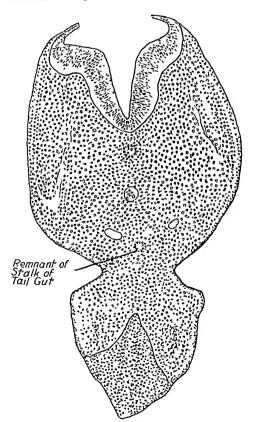
FIG. 220 —Transverse section through the tail end of a human embryo of 9 mm. showing remnant of stalk of tail gut. (75)

pouch corresponds roughly to the site of junction of the hind-gut and cloaca. The reflection of peritoneum from the anterior surface of the rectum marks the site of the former cloacal opening of the hind-gut.

Relation of the Primitive Streak.—In the invertebrate there is a circular opening in the gastrula-cavity called the blastopore. In forms higher than Amphibia the blastopore is replaced by the primitive streak, and these structures are thought to be homologous. In the later stages of gastrulation a sheet of mesoderm
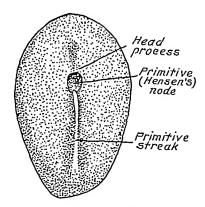
FIG. 221.—Blastoderm of rabbit embryo. (*After van Beneden—from Jordan and Kindred's ' Embryology'.*)

appears between the ectoderm and the unfolding entoderm and an oval plate is formed. In the mid-line of this oval mesodermal plate fusion occurs between the mesoderm and overlying ectoderm, and underlying entoderm. This
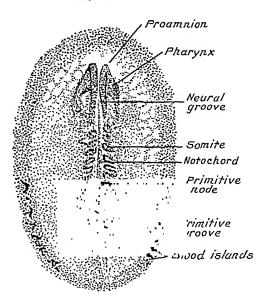
FIG. 222.—Chick embryo of 25 hours' incubation. (*A. Gurwitsch—from Jordan and Kindred's ' Embryology'.*)

line of fusion of three germinal layers is the primitive streak. Experimental evidence adduces that the major portion of the body is developed from the primitive streak. The embryo arises in the neighbourhood of the anterior end and the anus is formed at the posterior end. (*Figs.* 221, 222.)

Constituents of the Primitive Streak.—In the mid-line of the primitive streak is the primitive groove bounded laterally by the primitive folds. Caudally, the primitive folds become flattened out to form the primitive plate, whilst at the head end they become confluent and partially enclose the primitive pit. In the floor of the primitive pit a transient opening may develop between the underlying gut and the lumen of the neural tube ; this opening is the neurenteric canal. At the anterior aspect of the primitive streak is the primitive node, or Hensen's node. From the primitive node the primordium of the notochord grows forward in the mid-line. At the same time the primitive streak becomes shorter as if its tissues were being converted in part into notochord. Ultimately the primitive streak appears as a minute remnant to be incorporated in the tail bud.

PATHOLOGICAL STRUCTURES ON THE POSTERIOR ASPECT OF THE SACRUM AND COCCYX

Brief reference is made to certain cysts and sinuses which are encountered on the posterior aspect of the sacrum and coccyx. It is important to recognize the pathology of these abnormalities in order to institute the appropriate surgical treatment. The commonest lesion of this type is termed ' pilonidal sinus ', or sacro-coccygeal fistula. Bland-Sutton regarded the cause as faulty coalescence of the cutaneous covering of the back and compared the lesion with the interdigital pouch of the sheep. Newell states that the condition is a dermoid caused by traction of the underlying tissues on the median raphé when retrogression of the tail commences. The lesion presents an orifice 3 to 5 mm. in diameter in the posterior mid-line of the body at about the level of the sacro-coccygeal joint. Occasionally a small tuft of hair may be seen projecting from the orifice. The sinus passes in an upward direction for a variable distance towards the sacrum and terminates blindly without communicating with other structures. Histological examination of the sinus wall shows a lining of squamous epithelium, and therefore the appropriate treatment is complete surgical excision.

Miles has called attention to another type of fistula which results from a hæmatoma caused by a fall upon the buttocks. The aperture in these cases is almost invariably situated on the left side within half an inch of the upper extremity of the internatal cleft. Schmidt has described a sacral dermoid with several fistulous openings associated with a complex mesodermal tumour containing tubules lined by cylindrical cells. Mallory has described a glioma occurring in this region which he believed originated in the remains of the neural canal.

PATHOLOGICAL STRUCTURES ON THE ANTERIOR ASPECT OF THE SACRUM AND COCCYX

These may be classified as : (*I*) *Cysts*; (*II*) *Tumours*. They are dealt with in detail below.

I. CYSTS

1. DERMOID CYSTS

Dermoid cysts are composed essentially of derivatives of the ectodermal layer and commonly originate by the inclusion of a portion of ectoderm during coalescence of cutaneous surfaces or at the union of ectodermal with other structures. They

also occur along the course of ectodermal invaginations and from the persistence of embryological ectodermal structures. Dermoid cysts may be simple or complex. In the former the lining is columnar or squamous epithelium with or without skin appendages. In the complex variety various structures such as teeth are present.
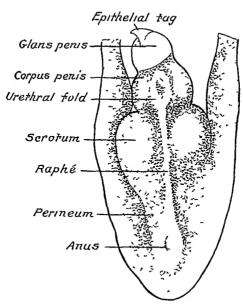
FIG 223 —The development of the external genitalia of the human male at 12 weeks (× 6)
(*After Spaulding—from Arey's ' Developmental Anatomy '*)

Skutsch has collected from the literature the records of seventeen cases of dermoid occurring in the pelvic connective tissue. The commonest site is between the rectum and sacrum, and the tumour may expand laterally or in a vertical direction. In some cases they are found on the lateral aspect of the rectum and in the ischiorectal fossa. Two cases were found to have cysts in the gluteal region.

FIG 224 —*Case 1* Dermoid cyst arising from the perineum (*Natural size*) (*R C S. Museum*, 1199 1)

Examples of Dermoid Cysts in the Region of the Rectum.—

1. *Arising from an Ectodermal Inclusion during Coalescence of Cutaneous Surfaces (Fig. 223).*—The following case is an example of this type :—

Case 1.—**Dermoid cyst from the perineum** (*R.C.S. Museum*, 1199.1).

HISTORY.—A bi-lobed cyst excised from the perineum near the perineo-scrotal junction of a male aged 13 years.
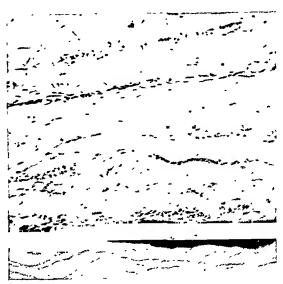
FIG. 225.—*Case* 1. Microscopic section of dermoid cyst from perineum. The cyst is lined with epidermis furnished with a stratum granulosum. (× 240.)
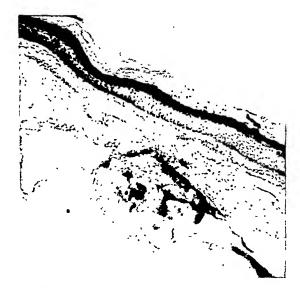
FIG. 226.—*Case* 2. Microscopic section of dermoid cyst from ischiorectal fossa. Wall of cyst lined with squamous stratified epithelium showing a well-marked stratum granulosum as in the epidermis. (× 75.)

NAKED-EYE DESCRIPTION.—A cyst composed of two loculi which communicate through a narrow channel (*Fig* 224). The cyst has a tubular pedicle about 2 cm. in length, which opened in front of the anus.

MICROSCOPICAL STRUCTURE (*Fig.* 225).—The cyst is lined with epidermis furnished with a stratum granulosum. The pedicle is also lined with well-developed epidermis showing papillæ. No hair follicles or glands are present.

2. *Arising in connection with the Proctodeum.*—An example of this type is given below :—

Case 2.—**Dermoid cyst from the ischiorectal fossa** (*R.C.S. Museum*, 1200.1).

HISTORY.—Cyst removed from the ischiorectal fossa of a boy in close proximity to the rectum.

NAKED-EYE DESCRIPTION.—A small spherical thin-walled cyst, 2·5 cm. in diameter. It was filled with desquamated epithelial cells.

MICROSCOPICAL STRUCTURE (*Fig.* 226).—The cyst is lined with squamous stratified epithelium showing a well-marked stratum granulosum as in the epidermis. Immediately beneath the epithelial lining are sparsely scattered, very obliquely disposed hair follicles.
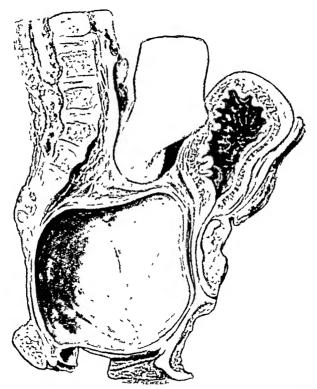
FIG. 227.—*Case* 3   Sagittal section through the pelvis showing a cyst arising from the sacro-coccygeal region. (× ⅔.) (*Museum of St. Bartholomew's Hospital*, L278.)

3. *Arising from the Neurenteric Canal.*—An example of a cyst arising in the sacro-coccygeal region is given below.

Case 3.—**Cyst from the sacro-coccygeal region** (*Museum of St. Bartholomew's Hospital*, L278).

HISTORY.—The pelvic organs of a child, aged 2 weeks, who died as a result of intestinal obstruction caused by a bluish-red fluctuating swelling protruding at the anus.

NAKED-EYE DESCRIPTION.—A sagittal section through the pelvis of a child showing a large cyst below the rectum, situated in front of the sacrum and coccyx and bulging into the anus (*Fig.* 227).   There is marked narrowing of the lumen of the rectum, which has been

laid open to show the obstruction. The cyst was filled with clear fluid. The large intestine was much distended and there was a small perforation in the cæcum; fæcal matter had passed into the peritoneal cavity.

MICROSCOPICAL STRUCTURE.—The cyst is lined with a single layer of flattened epithelium.

Galletly believes that simple pre-sacral cysts lined by squamous or columnar epithelium probably originate from cells of the neurenteric canal, which is an ectodermal invagination connecting the neural tube with the primitive hind-gut. He describes a cyst removed from the pelvis of a female aged 43 years. Microscopical examination showed a lining of squamous epithelium with areas of keratinization, and intracystic tufts composed of tubules lined by columnar cells of intestinal type.

Complex Dermoid Cysts in the Region of the Rectum.—Complex dermoid cysts are not common in the sacro-coccygeal region and are usually noticed before puberty. The following examples are therefore of interest :—

Case 4.—**Complex dermoid cyst** (*Museum of St. Bartholomew's Hospital*, L277).
HISTORY.—Cyst removed from a female, aged 39 years, who had experienced some inconvenience in assuming the sitting posture. On the occasion of her confinement the
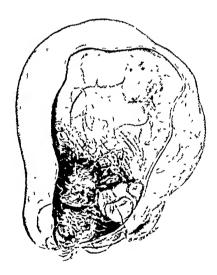
FIG 228.—*Case 4.* Complex dermoid cyst containing hair and teeth. (× ⅖.) (*Museum of St. Bartholomew's Hospital*, L277.)

head in its descent extruded the cyst through the anal orifice. The cyst was covered by the mucous membrane of the gut, the rupture of which permitted enucleation of the whole cyst.

NAKED-EYE DESCRIPTION.—A cyst containing two balls of hair (*Fig.* 228). There are two fairly well-formed teeth attached to its wall—one molar and one incisor. The cyst is pear-shaped and was attached by its apex.

Case 5.—**Complex dermoid cyst** (*Museum of Guy's Hospital*, 585).
HISTORY.—Cyst removed from the sacro-coccygeal region.
NAKED-EYE DESCRIPTION—The cyst has been opened and everted to show its cavity lined with skin to which are attached a few downy hairs (*Fig.* 229). There projects into

the cavity a rudimentary limb with three malformed digits, each of which bears a claw-like nail. Under the skin of the cyst there is a layer of fatty areolar tissue in which were embedded numerous pieces of bone.
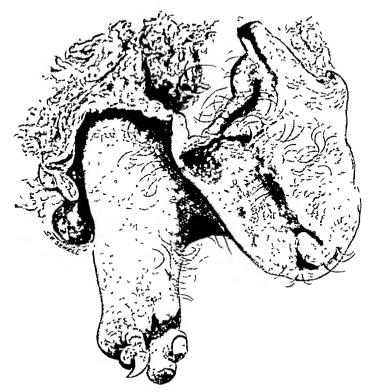
FIG. 229.—*Case 5.* Complex dermoid cyst containing hair and a rudimentary limb ($\times \frac{2}{3}$) (*Museum of Guy's Hospital,* 585)

2. CYSTS ARISING FROM THE EMBRYONIC POST-ANAL GUT

It has been shown that the developing anal canal joins the intestinal wall at some distance from the extremity of the intestine. Consequently a portion of the distal region of the intestine lying on the ventral surface of the coccyx is cut off from the intestinal canal and becomes atrophic. Attention was first directed to the pathology of the post-anal gut by Middeldorpf. He described a cystic tumour removed from a child of 1 year. The specimen was composed of fat, connective tissue, with layers of intestinal mucosa and mucous glands. Middledorpf was of the opinion that the cyst was derived from the post-anal gut, and this view concerning the origin of certain cysts and tumours has been supported by Keen and Bland-Sutton. Such cysts may be analogous to Meckel's diverticulum and to certain varieties of œsophageal diverticula encountered in the region of the bifurcation of the trachea.

The anatomical position of a derivative of the post-anal gut is on the posterior aspect of the rectum and anterior to the sacrum and coccyx. These cysts are lined with columnar epithelium, which in parts may be ciliated. Mucous glands of intestinal type may also be present.

Case 6.—**Cyst derived from the post-anal gut** (*Museum of St. Bartholomew's Hospital*, TE165).

HISTORY.—An infant of $2\frac{1}{2}$ months was admitted to hospital with acute intestinal obstruction, and an exploratory laparotomy was performed. The child died during the following day.

NAKED-EYE DESCRIPTION.—The specimen shows the pelvic organs together with the kidneys and ureters of a female infant (*Fig.* 230). An oval cyst, 5 cm. in its long diameter,
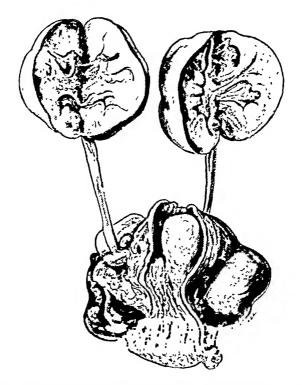
FIG. 230.—*Case* 6. Pelvic organs with kidneys and ureters of a female infant. ($\times \frac{2}{5}$.) (*Museum of St. Bartholomew's Hospital, TE165.*)

is attached to the posterior wall of the rectum. The cyst has been laid open to show the thickness of its walls. A small fibrous cord joins the lower part of the cyst to the posterior margin of the anus. The ureters and pelves of the kidneys are dilated owing to pressure of the cyst in the pelvis.

MICROSCOPICAL STRUCTURE.—The cyst is lined by several layers of cells, the innermost of which is columnar and ciliated.

3. SACRO-COCCYGEAL CYSTS OF MENINGEAL ORIGIN

The following is an example of this variety of cyst:—

Case 7.—**Sacro-coccygeal cyst of meningeal origin.**

HISTORY.—Specimen removed from a post-mortem subject, death occurring from other cause. This was investigated by kind permission of Professor G. Hadfield.

NAKED-EYE DESCRIPTION.—The specimen (*Fig.* 231) shows the sacrum and coccyx. The first sacral foramina are abnormally large and permit the passage of two large cysts

derived from the meninges of the spinal cord.   The larger cyst on the right side is traversed by several nerves.

MICROSCOPICAL STRUCTURE —The cysts are lined by flattened cells   A small piece of bone is present in the wall of the larger cyst
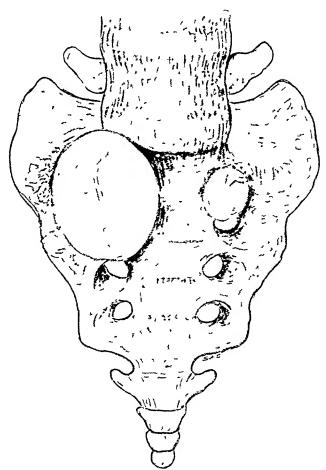
FIG 231 —*Case* 7   Sacro coccygeal cyst of meningeal origin

II. TUMOURS

A survey of the literature shows what a diversity of tumours have been found in the sacro-coccygeal region.   Practically all types of tumours are represented here.   They may be divided as follows :—

SACRO-COCCYGEAL TUMOURS

1. Innocent
    a. Lipoma
    b. Fibroma
    c. Myoma
    d Chondroma
2. Glioma derived from ependymal cells
3. Neuroblastoma
4. Chordoma

5. Tumours associated with spina bifida
6. Teratoid tumour
7 Teratoma
8 Parasitic fœtus
9. Sarcoma
10 Carcinoma
11. Endothelioma

It is important that sacro-coccygeal tumours be considered in the differential diagnosis of other swellings occurring in the pelvis, such as fibroid tumours of the uterus, cysts of the ovary, tubal and abdominal pregnancy, pelvic abscesses, intraligamentous cysts, and anterior spina bifida.

TERATOMATA

This type of tumour appears to be the commonest variety occurring in the sacro-coccygeal region. As in the case of teratoma in general, there are numerous hypotheses held concerning their genesis. In an excellent paper Nicholson has drawn attention to the possibility of tumour formation being the expression of an inherent and physiological reaction of the individual. He states that tumours are pathological manifestations of physiological growth. The activities of a tumour are always reducible to the physiological reactions which underlie somatic growth in spite of their erratic and autonomous nature. The solution to the problem of tumour formation will probably not come until more precise knowledge is available concerning physiological growth. In this connection important contacts are being made between pathology, physiology, and the developing science of experimental embryology. One cannot escape being impressed with the importance of the discoveries in this new field which is being prospected and opened up—discoveries that are concisely set out in a recent publication by Huxley and De Beer.

The Nature of Teratomata.—Until recent years our knowledge of the nature of teratomata has been very poor. Light has been thrown on the problem by Budde (1921), Nicholson (1929), and Willis (1935).

Homology with Distorted Fœtus.—It has been said that a teratoma is really a distorted fœtus. Recent opinion holds that this view is untenable. An embryo is a viable and independent individual, whereas a teratoma is a part of the body of its host. Willis points out that in a teratoma the fundamental features of the formation of a soma are not present—that is, there is no evidence in the tumour of axiation, metameric segmentation, or delamination of germ layers. There is no topographical arrangement of tissues in a teratoma such as is seen in the fœtus ; there are numerous intestinal cysts, but no real alimentary canal can be found ; there is abundance of nervous tissue, but no well-developed brain is present; masses of bone may be seen, but no named bone can be identified.

If the view is accepted that a teratoma does not represent a distorted fœtus, the two further hypotheses must automatically be rejected—of twin-inclusion and parthenogenesis. Imperfect twins and parthenogenic organisms do not reveal the absence of axiation and segmentation which is seen in most teratomata.

Tissue Correlations in Teratomata.—This subject has been admirably worked out recently by Nicholson and Willis. In these tumours is demonstrated the physiological stimulus which is exerted by one tissue on another.

Tooth Formation in Teratomata.—Tooth formation in these tumours shows a sequence of correlations similar to those of normal ontogeny. The invaginated enamel organs stimulate the formation of dental papillæ in the mesenchyme from which develops odontoblastic tissue and pulp. Bone may even be formed around these developing teeth, and structures like the maxilla may be formed.

Respiratory Epithelium and Cartilage.—It is very probable that respiratory epithelium stimulates surrounding mesenchyme and this reacts to the physiological stimulus with the production of cartilage.

Glandular Epithelium and Smooth Muscle —When smooth muscle is present in teratomata it is generally associated with glandular acini. Willis states it appears that particular kinds of epithelia growing amongst indifferent mesenchyme induces the latter to form muscle, and he describes the genesis and growth of these organoid
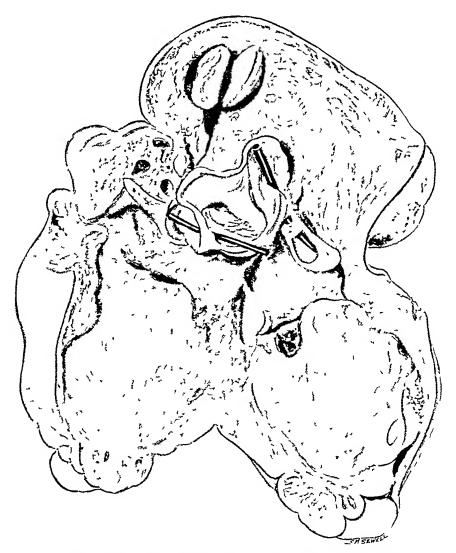
FIG 232 —*Case* 8   Sacro coccygeal teratoma   (× ⅔)   (*R C S   Museum*, 1549 1)

formations through all stages. He pertinently expresses a suspicion that the same inductive influence of epithelium is responsible in normal ontogeny for the develop-ment of muscle in the walls of the viscera.

Examples of Sacro-coccygeal Teratomata.—The following nine cases are examples of sacro-coccygeal teratomata :—

Case 8.—**Sacro-coccygeal teratoma** (*R.C.S. Museum*, 1549.1).

HISTORY.—Tumour removed from the nates of a child aged 2 years.

NAKED-EYE DESCRIPTION.—An irregular oval tumour partly bisected, 11·5 cm. in its chief diameter (*Fig.* 232). In the upper part a piece of intestine 7·6 cm. in length has been dissected out; this is blind at one end, and originally contained fluid resembling meconium. Above this on the left a few nodules of cartilage are present. On the outer side there is a more or less isolated lobe in which are scattered cystic cavities.

FIG. 233.—*Case* 8. Microscopic section of sacro-coccygeal teratoma. The section shows dense fibrous tissue with a few nerves present with a small amount of smooth muscle fibres. An extensive cleft is shown lined with columnar epithelium but without any proper wall. (× 240.)

MICROSCOPICAL STRUCTURE (*Fig.* 233).—The main mass of tumour consists of dense fibrous tissue intermixed with fat. The isolated lobe on the outer aspect of the tumour consists of fibrous tissue with intervening zones of mucous tissue from which fat is forming. Extensive clefts are present, lined with columnar epithelium but without any proper wall. A few well-formed nerves are present and there is a small amount of smooth muscle fibres.

Case 9.—**Sacro-coccygeal teratoma** (*R.C.S. Museum*, 1550.1).

HISTORY.—Tumour removed from the gluteal region.

NAKED-EYE DESCRIPTION.—The greater part of the tumour consists of a large multi-locular smooth-walled cyst at its free end, and of other cysts at its superior extremity (*Fig.* 234). The two larger cysts were filled with fatty material; amongst this were a few short dark hairs. Behind the largest of the upper cysts is a short blind coil of gut. On the posterior aspect of the tumour there are two areas of pigmented skin, and in the centre of the lower area is the orifice of a canal 2·5 cm. in length.
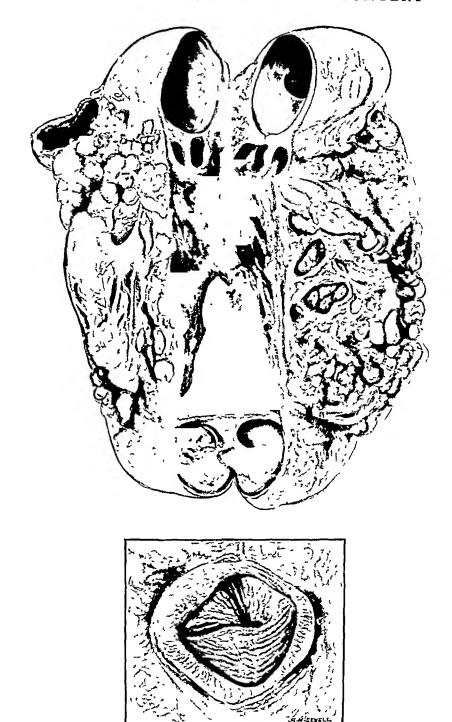
Fig 234.—*Case* 9.   Sacro-coccygeal teratoma.   × ½.)   (*R C S. Museum*, 1550 l.)

MICROSCOPIC STRUCTURE (*Figs.* 235, 236).—The epithelium of the blind coil of gut is glandular and resembles gastric mucosa in parts; other portions show intestinal type of

FIG. 235.—*Case* 10. Microscopic section of sacro-coccygeal teratoma showing epithelium composed of columnar cells resembling that of the large intestine. Numerous goblet cells are visible. (× 240.)
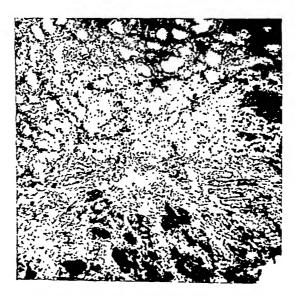
FIG. 236.—*Case* 10. Microscopic section of sacro-coccygeal teratoma showing glandular epithelium resembling gastric mucosa. (× 75.)

epithelium. Beneath this epithelium there are small nodules of bone and cartilage and also a small lymph gland.

Case 10.—**Sacro-coccygeal teratoma** (*R.C.S. Museum*, 1550.2).

HISTORY.—Child born with a large tumour attached to the tip of the coccyx. The anus was rudimentary, and fæces were passed through the vulva.

NAKED-EYE DESCRIPTION.—Half of a bi-lobed tumour measuring 16 cm. in its longest diameter (*Fig.* 237). As displayed, it shows two cysts of about equal size consisting of skin with a thin proper wall adherent to it. A somewhat pedunculated solid growth projects into each cyst. The intracystic growth consists of connective tissue in which lies an abundance
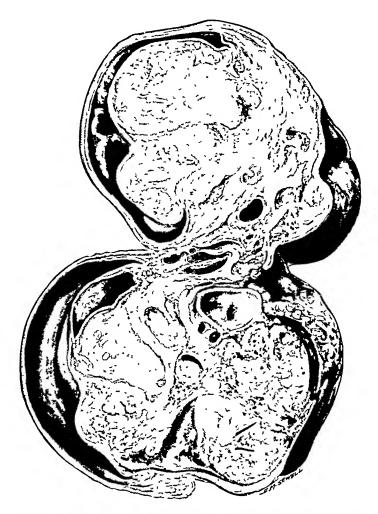
FIG. 237.—*Case* 10. Sacro-coccygeal teratoma. (× ⅖.) (*R.C.S. Museum*, 1550.2.)

of finely lobulated white fat. In the connective tissue there are embedded a few small islets of cartilage and bone; one of these is indicated in the lower segment of *Fig.* 237 by two black bristles. A certain number of well-defined, thin-walled cysts are distributed in the two tumours, especially about their bases of attachment. One of these cysts contains a few slender dark hairs.

MICROSCOPICAL STRUCTURE.—The main mass of the tumour consists of simple adipose and connective tissue. The cysts are lined with columnar epithelium which is ciliated in parts. Some of these cysts are papilliferous, showing intestinal villi and crypts. In the

fibrous tissue adjoining the crypts are sharply defined areas of neuroglia. Strands of unstriped muscle run in the course of some of the fibrous septa, but without any definite relation to the cystic spaces.

Case 11.—**Sacro-coccygeal teratoma** (*R.C.S. Museum*, 1550.3).

HISTORY.—Tumour removed together with the coccyx from the sacro-coccygeal region of a child aged 2½ years.

NAKED-EYE DESCRIPTION.—The cut section of the tumour shows a preponderance of fat which is closely connected in its deepest part with the coccyx and is covered superficially with normal skin.

MICROSCOPICAL STRUCTURE.—The tumour consists of fat, striped muscle fibres, and nerve bundles.
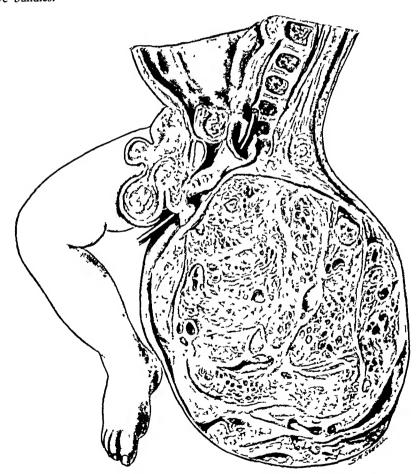
FIG. 238 —*Case* 12. Sacro-coccygeal teratoma (× ½) (*R C S Museum*, 1545 1)

Case 12.—**Sacro-coccygeal teratoma** (*R.C.S. Museum*, 1545.1).

HISTORY.—The infant was born with the tumour, and died at the age of 6 weeks.

NAKED-EYE DESCRIPTION.—The specimen shows the right half of the lower part of the body of an infant (*Fig.* 238). The rectum and lower part of the sacrum and coccyx are widely separated by a large oval tumour 14 cm. in its chief vertical diameter. The tumour

is everywhere sharply circumscribed and is minutely cystic throughout. It is imperfectly subdivided into lobes by strands of connective tissue.

MICROSCOPICAL STRUCTURE.—The tumour is composed of spaces lined with cubical or columnar epithelium. In the intercystic partitions branching plates of hyaline cartilage are present which have undergone ossification in places.

Case 13.—**Sacro-coccygeal teratoma** (*R.C.S. Museum*, 1546.1).

HISTORY.—A female infant was born with a large sacro-coccygeal tumour. The specimen was obtained when the child was aged 3 months.

NAKED-EYE DESCRIPTION.—One half of a vertical section of a large congenital sacro-coccygeal tumour. A portion of the tumour projected backwards behind the apex of the coccyx. The coccyx is displaced posteriorly. The tumour is imperfectly divided into lobes of considerable size, all of which are finely spongy or more coarsely cystic. In the recent state the spaces contained a glairy transparent fluid.
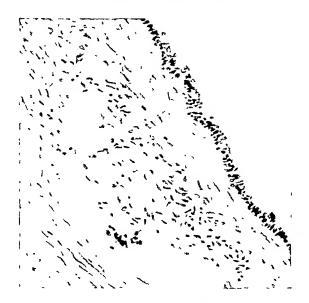
FIG. 239.—*Case* 13.   Microscopic section of sacro-coccygeal teratoma.   Lining of cystic space composed of columnar epithelium.   The stroma is very cellular.   (× 240.)

MICROSCOPICAL STRUCTURE (*Fig.* 239).—The complex structures are lined with columnar epithelium. The stroma is fairly abundant and very cellular; in parts it is mucous and contains groups of fat cells. There are small well-defined areas of hyaline cartilage sparsely distributed in the stroma.

Case 14.—**Sacro-coccygeal teratoma** (*R.C.S. Museum*, 1838.1).

HISTORY.—A premature child born with a sacro-coccygeal tumour.

NAKED-EYE DESCRIPTION.—A sagittal section of the lower part of the trunk of a premature child (*Fig.* 240). Between the sacrum and coccyx and the rectum there is an ovoid tumour, 7·5 cm. in chief vertical diameter. The tumour is intimately connected with the skin and is of particularly soft consistence though supported by somewhat coarse processes of connective tissue. It contains a few well-defined cysts, certain of which appear to have ruptured on the posterior surface, and has led to the production of external depressions. Immediately on the hinder wall of the rectum, below its middle, there is a small, minutely cystic area of glandular character; similar areas may be found towards the posterior border of the tumour.

MICROSCOPICAL STRUCTURE (*Fig.* 241).—Cystic areas are present which are lined with columnar epithelium. These cysts are dilated to form channels. The stroma contains

nervous tissue in which large branching nerve cells are distributed. A few small well-defined processes of hyaline cartilage occur in the midst of the supporting tissue. Between the glandular elements are small groups and lines of fat cells.

FIG. 240.—*Case* 14. Sacro-coccygeal teratoma. (× ⅔.) (*R.C.S. Museum,* 1838.1.)
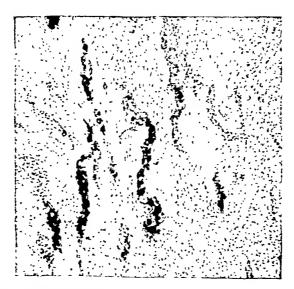
FIG. 241.—*Case* 14. Microscopic section of sacro-coccygeal teratoma showing well-defined processes of hyaline cartilage in the midst of supporting connective tissue. (× 75.)
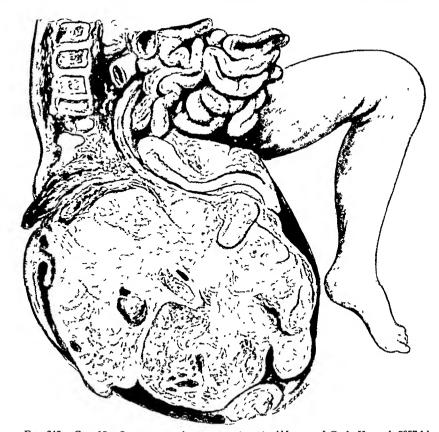
Fig. 242.—*Case* 15.   Sacro-coccygeal teratoma.   (× ⅛.)   (*Museum of Guy's Hospital*, 5857.1.)

Fig 243.—*Case* 15.   Microscopic section of sacro-coccygeal teratoma showing papillary processes
covered with columnar epithelium.   (× 240)

Case 15. **Sacro-coccygeal teratoma** (*Museum of Guy's Hospital*, 5857.1).

HISTORY.—A full-term child born with a sacro-coccygeal tumour.

NAKED-EYE DESCRIPTION.—A sagittal section through the pelvis of a full-term child
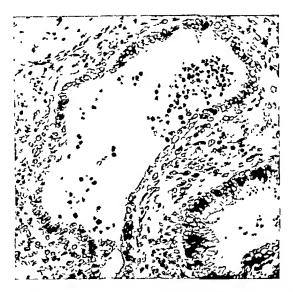
FIG. 244.—*Case* 15. Microscopic section of sacro-coccygeal teratoma showing cystic spaces lined with single layer of columnar epithelium. (× 240.)
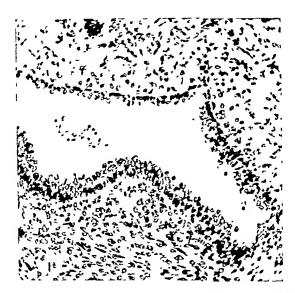
FIG. 245.—*Case* 15. Microscopic section of sacro-coccygeal teratoma showing large cystic cavity lined with columnar epithelium which is several layers thick in parts. (× 240.)

(*Fig.* 242). The anus is displaced forward by a globular tumour 10 cm. in diameter lying between the coccyx and anus and projecting from the perineum. The rectum is stretched over the upper aspect of the tumour, and the rest of its surface is covered by perineal skin

which is œdematous in its lowest part. The tumour is strictly encapsuled and but loosely attached to the surrounding structures. The consistency is soft and the cut surface is beset with numerous small cysts.

MICROSCOPICAL STRUCTURE (*Figs.* 243-245).—Numerous cystic spaces are seen lined by three different types of columnar epithelium. The matrix is composed of loose fibrillary tissue in which are numerous masses of hyaline cartilage.

Case 16.—**Malignant sacro-coccygeal teratoma** (*Museum of St. Bartholomew's Hospital,* L276A).
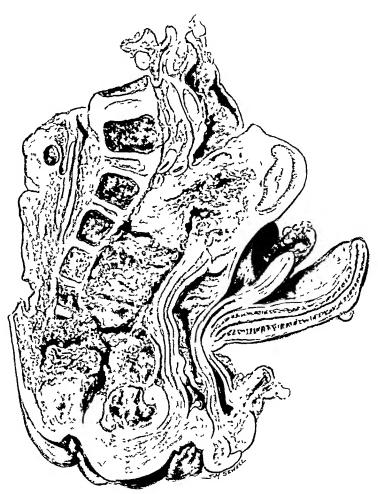
FIG. 246.—*Case* 16. Malignant sacro-coccygeal teratoma. (× ⅓.) (*Museum of St. Bartholomew's Hospital,* L276A.)

HISTORY.—The child was aged 2 years and apparently well until five weeks before death, when it was noticed that a bluish swelling had developed on the left buttock. The patient had been constipated. On admission to hospital a firm elastic swelling was found situated on the left side of the anus, and the urinary bladder was distended. The swelling was incised and about 2 oz. of blood-clot and degenerated tissue were evacuated.

NAKED-EYE DESCRIPTION.—A sagittal section through the pelvis of a child showing a friable tumour situated between the sacrum and rectum (*Fig.* 246). It extends upwards to

the level of the fifth lumbar vertebra. Inferiorly it causes a swelling in the left buttock where an incision has been made. The lower segments of the sacrum and coccyx are eroded and the rectum is pushed forward. The urethra is elongated and the bladder displaced upwards. The lower part of the tumour is hæmorrhagic, the middle is brown in colour, and the upper part is paler. There are a number of small cystic spaces present.

MICROSCOPICAL STRUCTURE.—The tumour consists chiefly of irregular cells with pale cytoplasm, and the nuclei show mitotic figures. There is an attempt on the part of the cells to form alveoli. Interspersed amongst the cellular elements are plain muscle fibres.

In the present state of our knowledge of tumours in general and of teratomata in particular, it is impossible to state the origin of sacro-coccygeal teratomata. It appears true, as Nicholson suggests, that they are malformations. Further knowledge of their origin will be gained as experimental embryology unravels the intricacies of the complex developmental processes and throws new light on the growth centres of the body situated at the caudal extremity. It may be that these malformations will prove to be due to a faulty coherence of embryonal parts and a diminution of growth momentum.

PYLEPHLEBITIS COMPLICATING APPENDICITIS AND ITS TREATMENT BY LIGATURE OF THE MESENTERIC VEINS

BY A. M. STEWART-WALLACE

MEDICAL FIRST ASSISTANT AND REGISTRAR, LONDON HOSPITAL

THE following case is reported by kind permission of Mr. Julian Taylor :—

An unmarried girl, age 18, was admitted on March 1, 1932, into University College Hospital with a three days' history of abdominal pain and vomiting, and having obvious signs of general peritonitis.

FIRST OPERATION.—By Mr. Julian Taylor under open ether anæsthesia. Battle's incision. Pus was present in the general peritoneal cavity and welled up out of the pelvis (grew *B. coli* and non-hæmolytic streptococci). The appendix was gangrenous and perforated. It was found below and posterior to the cæcum and was removed. Large rubber drainage tube into pelvis.

The patient was nursed in Fowler's position : 30 c.c. of antiscarlatinal serum and 30 c.c. of double-strength saline were given intravenously. Rectal salines.

March 4.—The general condition was satisfactory. The drainage tube was removed. There was one slight rigor in the evening.

March 5.—The patient complained of occasional colicky pains in the centre of the abdomen. Two definite rigors occurred. There were no physical signs in the chest or abdomen, and no pus-cells or organisms in the urine.

March 6.—There were frequent attacks of severe colicky abdominal pains, much worse after taking any fluids, including water. Bowels not open, no vomiting. One severe rigor in the afternoon. The patient had a dry furred tongue, rapid pulse, and was sweating profusely. There was no jaundice of skin or conjunctivæ, and the heart and chest were normal. There was tenderness on the right side of the abdomen over an area stretching from the appendicectomy wound to half-way between the umbilicus and the right costal margin. No marked rigidity. The edges of the wound were red and inflamed and the sinus was discharging foul-smelling pus. The lower border of the liver was tender on palpation. P.R., nil abnormal.

The patient was seen by Mr. Julian Taylor, who made a pre-operative diagnosis of ascending mesenteric thrombophlebitis and portal pyæmia, and advised immediate laparotomy.

SECOND OPERATION.—By Mr. Julian Taylor under open ether anæsthesia through a right paramedian incision. The general peritonitis had settled down. The superior mesenteric vein was thrombosed from the extreme radicles supplying the cæcal area to within ¾ in. of its junction with the splenic vein. The vein was hard, about the size of the little finger, and covered with flakes of lymph. The splenic and portal veins were unaffected. The liver was engorged and swollen. No evidence of infarction of any part of the intestine. The upper part of the superior mesenteric vein was approached through the posterior layer of the transverse mesocolon and exposed, the right colic artery being tied in the process. The superior mesenteric vein was ligatured immediately proximal to the upper limit of the thrombus. Sudden marked engorgement of all the colic veins was at once apparent as the ligature was tightened. The abdomen was closed without drainage. One pint of intravenous saline was given in the theatre. The patient was extremely shocked, but had recovered considerably one hour later after treatment with warmth, raised lower extremities, and injections of camphor and strychnine ; 20 c.c. of antistreptococcal serum were given.

SUBSEQUENT PROGRESS.—The general condition had greatly improved on the following day. There were no further rigors and the hepatic enlargement and tenderness gradually
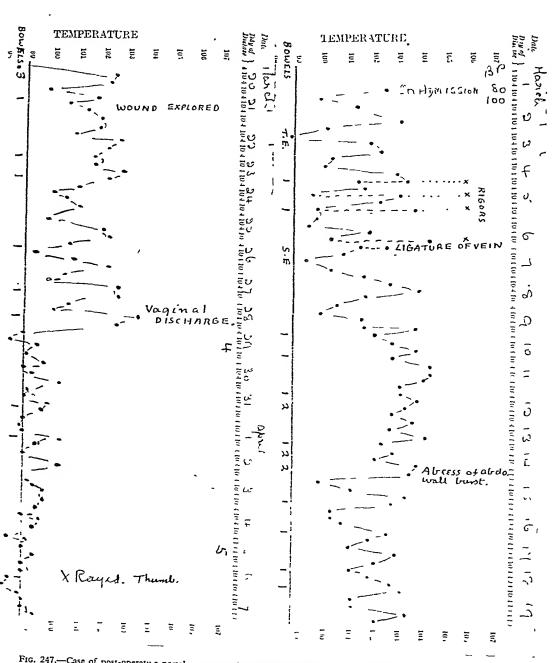
FIG. 247.—Case of post-operative portal pyæmia and ascending pylephlebitis, successfully treated by ligature of the superior mesenteric vein.

subsided. No gross intestinal disturbances were apparent. The colicky abdominal pains of which she had previously complained continued during the next two or three days. A normal result followed an enema on the first day, but thereafter the bowels opened normally; the motions were of normal colour, never loose, and did not contain visible blood.

Her convalescence was complicated by development of pus between the layers of the anterior abdominal wall and a pelvic abscess which finally burst into the vagina. Rapid and complete recovery then followed (*Fig.* 247), and she was discharged on April 26 very fit, free of symptoms, and with her abdominal wounds completely healed. She later returned to work, and during the last three years has remained very well except for occasional slight dyspepsia and mild constipation.

EFFECTS OF OCCLUSION OF THE MESENTERIC VEINS

From experimental ligations on animals it would appear that ligature of the most proximal part of the trunk of the superior mesenteric vein usually produces necrosis of the whole small intestine from the middle of the duodenum to the cæcum; tying the large and medium-sized tributaries, except in large numbers,
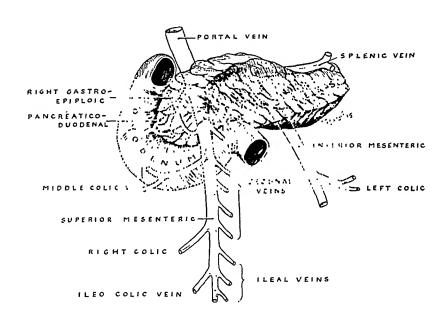
FIG. 248.—The tributaries of the superior mesenteric vein as they are commonly found; the exact arrangement is subject to variation in different individuals.

rarely leads to gross intestinal lesions; while in the case of small radicles in the mesentery close to its line of attachment to the intestine, necrosis usually occurs.

L. B. Trotter found that of 103 cases of superior mesenteric vein thrombosis in man, in which the main trunk was involved, infarction occurred in 70 (68 per cent); and of 34 cases when tributaries only were affected, in 21 (63 per cent) there was infarction. When infarction did not take place the changes found were

œdema, engorgement, hæmorrhage, and ulceration, and, in some slight cases, no intestinal lesion. Though it is not stated precisely to what degree the trunk was involved or how far proximal the thrombus extended, these findings show that the circulation can be carried on even if a large part of the mesenteric venous system has undergone thrombosis. No intestinal infarction occurs so
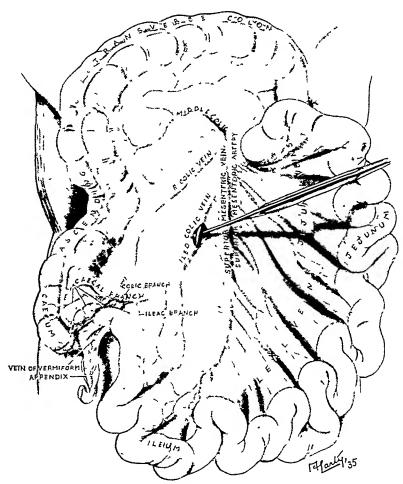
FIG 249.—The superior mesenteric vein and its tributaries draining the appendix area, showing the ileocolic vein isolated preliminary to passing a ligature. (*See p 372*)

long as the anastomotic arcades and their radicles remain free and some tributaries opening into the vein above the clot are patent. The most extensive thrombosis only leads to lesions confined to a small region of the bowel, that sector in which the thrombosis has spread to involve the anastomotic arcades and their radicles.

The results of ligature of the superior mesenteric vein in man are interesting. Two cases are on record (Robson, 1897, and Wilms, 1901) of traumatic laceration of the main trunk of the vein at the level of the root of the transverse mesocolon, where ligation was followed by complete recovery. Sudeck, Colp, and Braunig each record a case of ligature of the superior mesenteric vein for post-appendicular thrombophlebitis, and though the latter two died from liver abscesses six weeks later and peritonitis two days later respectively, no intestinal infarction occurred. Including our case, therefore, we have been able to collect six instances of ligature of the superior mesenteric vein in man, and no serious damage to the bowel appears to have resulted. The four which completely recovered have suffered no lasting ill effects and a satisfactory collateral circulation must have been established.

Now in all these cases the ligature was applied in the region of the transverse mesocolon and the third part of the duodenum. Though the exact relations of the ligature to the entrance of the various tributaries in this neighbourhood were not accurately known or stated, and though the precise arrangement of the veins varies in different individuals, it will be seen from *Fig.* 248 that the right gastro-epiploic, the pancreatico-duodenal, some of the upper jejunal veins, and in some or all of the cases the middle colic vein, must have opened into the vein proximal to the ligature. The ligature, therefore, has not been applied strictly to the ' trunk ' of the vein corresponding to the fatal animal experimental ligatures mentioned. We can conclude, therefore, that it is possible to tie the superior mesenteric vein at or below the level of the transverse mesocolon and third part of the duodenum. But at a higher level, where it is in relationship with the pancreas, animal experiments suggest that necrosis of the whole small intestine would probably result ; care must be taken, therefore, not to injure the vein in carrying out operations on the pancreas.

In our case, as the ligature was tightened all the colic veins were seen to distend, and the venous return from the colon must have taken place by way of the anastomotic channels to the middle colic, and round to the left colic into the inferior mesenteric vein ; and from the small intestine by way of the upper jejunal, the pancreatico-duodenal, and right gastro-epiploic veins (*see Figs.* 248, 249).

In none of 21 cases in which the ileocolic vein has been ligatured did intestinal necrosis occur. However, ligature of the small veins in the cæcal angle distal to the anastomotic arcade was not without danger ; thus a fæcal fistula followed a case described by Sprengel.

THE EARLY SYMPTOMS OF PORTAL PYÆMIA COMPLICATING TYPHLITIS

The diagnosis of portal pyæmia immediately after its onset is such an essential part of any prophylactic measure against pylephlebitis that a careful study and an appreciation of the significance of the earliest signs are of the greatest importance. The condition will present itself as : (1) An acute abdomen with additional rigors and perhaps evidence of hepatic involvement. The signs of the appendicitis may be obvious, or more frequently are atypical and confused by the pyæmic symptoms. (2) A post-operative complication following laparotomy for appendicitis.

An analysis of the five fatal cases of pylephlebitis (*see* p. 373) and Julian Taylor's case of thrombophlebitis of the superior mesenteric vein and engorged swollen liver, which occurred in the course of 5741 cases of appendicitis admitted into the London and University College Hospitals during the last five years, shows that the ages varied from 17 to 38; 5 were male and 1 was female. Two were operated on within twenty-four hours of the onset of symptoms, and one each on the 2nd, 4th, 9th, and 12th days respectively. Multiple pre-operative rigors and tenderness in the right hypochondrium were present in both the latter two, while in one other a single pre-operative rigor had occurred. It is of interest to note that *Case* 2 was operated on within twenty-four hours and *Case* 6 within twelve hours after the symptoms had begun, as it has been frequently stated, particularly by German writers, that pylephlebitis never occurs if the patient is operated on during the first twenty-four hours. A gangrenous appendix was found in all, two of which had ruptured, producing general peritonitis, and the two with the history of over a week had formed appendix abscesses. A fairly high intermittent pyrexia continued after operation, and in those with pyæmic symptoms previous to admission the rigors continued. In the other cases rigors started on the 2nd, 4th, and 15th day after operation respectively. Death resulted in one case in five days, but all the others lived from three to ten weeks after operation.

Of all the early symptoms that indicated that portal pyæmia was complicating the appendicitis the onset of rigors was undoubtedly the most outstanding feature in every case. Abdominal pain is almost always present according to the literature (Langdon-Brown). It is usually said to be the initial symptom, but it may follow one or two rigors. Beginning of inflammation of the portal vein or its tributaries is marked by the onset of pain. Von Schüppel (1880) believed that from its position the exact portion or factor of the vein affected may be determined. In our case colicky abdominal pains occurred on the morning following the first slight shivering attack. The pain was made worse by taking anything by mouth, even water, and gradually increased in intensity. On the next day examination revealed tenderness spreading up from the appendix region to half-way between the umbilicus and costal margin, the area corresponding to the portions of ileocolic and superior mesenteric veins found affected at laparotomy. Tenderness and enlargement of the liver, particularly the former, is present in most cases, but may not develop till a later stage. The liver edge was palpable and tender on the second day after the onset of rigors in Taylor's case, and also on admission in both the cases which had pre-operative pyæmic symptoms. Jaundice is present in less than 50 per cent of cases and often appears late (Lett); it was present in only one of our cases, being first noticed on the fifteenth day. One or more intestinal symptoms, such as furring of the tongue, nausea, vomiting, diarrhœa, or constipation, are usually present.

During the first two or three days, therefore, the stage at which, for our purposes of prophylactic treatment, it is essential to make the diagnosis, the onset of irregular rigors in a case of appendicitis is the outstanding diagnostic feature, and may, indeed, be the only symptom. This should always at once suggest portal pyæmia. Abdominal pain usually occurs if there is thrombosis of the mesenteric veins. Tenderness in the hypochondrium, a palpable tender liver, and occasionally jaundice, may be present and help to make the diagnosis more certain.

DIFFERENTIAL DIAGNOSIS : THE SIGNIFICANCE OF RIGORS

Since rigors may be the only definite sign at this early stage, it is obviously of the utmost importance to understand the significance of rigors complicating appendicitis. Undoubtedly their incidence used to be greater. Thus in Kelly and Hurdon's *Vermiform Appendix and its Diseases* (1905), it is stated that 50 per cent of cases of appendicitis with abscess formation or peritonitis have rigors, a figure which would certainly not apply to the cases admitted into a general hospital to-day. The earlier operation now practised has probably led to this decrease in their incidence, together with a corresponding decrease in the occurrence of pylephlebitis. Langdon-Brown found pylephlebitis in 6 per cent of 42 necropsies on typhlitis in St. Bartholomew's Hospital in the years 1893–8, as opposed to 2·6 per cent of 187 fatal cases from our series in 1930–4. Colp in 1927, in a series of 2841 cases of appendicitis at Mt. Sinai Hospital, New York, in which the presence or absence of chills had been specifically inquired for at the time of taking the histories, found pre-operative rigors in 6·8 per cent, the percentage being the same whatever the severity of the inflammation, whether catarrhal, gangrenous, or with localized or with general peritonitis. The death-rate in those with only one rigor was no higher than in those without, but of those in which two or more occurred, of which there were 11 cases (0·39 per cent), 5 died, 4 from pylephlebitis. Moreover, 88 per cent of the cases which developed pylephlebitis gave a history of pre-operative rigors. It appears, therefore, that one rigor before operation is of little significance, but that cases with multiple rigors must be regarded as potential cases of pylephlebitis.

Post-operative rigors, however, were extremely rare, especially where no pre-operative rigors had occurred, this happening in only 3 out of 2841 cases. Two of these died of pylephlebitis, and the other recovered without the cause being discovered. In our series of 5741 cases, post-operative rigors occurred in 8. Six had pylephlebitis, and of the other two, one (*Case 4*) had post-operative pyrexia for thirty days, with a rigor on the seventeenth, and recovered without the exact cause being discovered ; the other (*Case 3*) had an intermittent pyrexia for ten weeks, with frequent rigors from the seventeenth to the thirtieth day and a non-hæmolytic streptococcus in the blood ; there was no other evidence of portal pyæmia such as signs of hepatic involvement, in spite of the repeated rigors over a long period. Post-operative rigors are, therefore, very rare (1·3 per 1000 cases), and in 8 out of the 11 cases were proved to be due to portal pyæmia and pylephlebitis.

Cholecystitis.—In those cases which have not yet been operated on and in which the signs of the appendicitis are not obvious, the pylephlebitis is most easily confused with cholecystitis on account of shivering attacks, tenderness in the right hypochondrium, and possibly jaundice ; both the cases with pre-operative pyæmic symptoms were in fact diagnosed as cholecystitis, the appendix abscess in one case being in the pelvis, and in the other high up behind the ascending colon.

General Pyæmia and Septicæmia.—In *Case 1* repeated rigors occurred for fourteen days following laparotomy, but there were no signs of hepatic involvement and a non-hæmolytic streptococcus was grown on blood culture. The patient recovered and the condition would appear to have been a generalized systemic blood infection. Brutt reports a similar case of recurrent rigors, which also recovered, with *B. coli* on blood culture. The exact relationship between the infection of the general

blood-stream and the appendicitis is not obvious. It is generally held, though little definite evidence has been brought forward to support it, that the liver acts as a filter to the bacteria, and that a positive blood culture is rarely found in portal pyæmia unless there is a focus already established in the liver, which is in its turn feeding the systemic blood-stream. In *Case* 6 the blood culture was negative though repeated rigors had been occurring for many days. *B. coli* were grown from the blood of *Case* 3, but this was at a late stage, when probably the liver abscesses were well established and giving rise to systemic pyæmia and the multiple lung abscesses and meningitis which were found post mortem. Both the cases of septicæmia had peritonitis, and it is possible that direct infection of the systemic blood took place. On the other hand, the appendicitis may be a localized focus of infection secondary to the blood infection. It is certain, however, that onset of rigors is much more likely to be evidence of portal pyæmia, though occasionally an organism may be grown from the blood at an early stage, in which case the prognosis appears to be better.

Subphrenic Abscess.—The abdominal pain and tender hepatic swelling may cause confusion with subphrenic abscess. However, in Barnard's classical analysis of 76 cases, rigors occurred in only 10, all of which had further complications; 5 pyæmia, 1 cholangitis, 1 periostitis of a vertebra, and 2 a large perigastric abscess communicating with the stomach. Rigors as the presenting symptom are, therefore, unlikely to be evidence of an uncomplicated subphrenic abscess. Should shivering attacks be the initial symptom, it is probable that the subphrenic abscess is secondary to a liver abscess as in *Case* 6 and in one of Barnard's. Recently a case was seen of post-operative pyrexia with onset of rigors after a laparotomy for a perforated duodenal ulcer. There was dullness and diminished breath-sounds at the left base, and a radiograph showed a raised immobile diaphragm. A subphrenic abscess was found on exploration, but autopsy subsequently revealed, as was suspected from these observations on the significance of rigors, multiple abscesses in the liver in addition.

PROPHYLACTIC TREATMENT BY LIGATURE OF MESENTERIC VEINS

Gerster in 1903 advocated exposure and evacuation of thrombosed veins in the mesenteriolum and over the cæcum at the time of appendicectomy in cases of rigors when thrombophlebitis of these veins was found, and reported two successful cases where this procedure had been adopted. He admitted, however, that " on account of the anatomical relations this is sometimes easy, oftener difficult, and mostly impossible ".

Wilms in 1907 suggested ligation of the veins in the ileocolic angle, after separating the lower part of the ascending colon from the posterior abdominal wall by inserting a finger under its lateral aspect. He carried this out with a succesful result on a patient who was having recurrent rigors subsequent to drainage without appendicectomy three days previously for an appendix abscess with rigors. However, it is almost impossible to tie off all the veins in the ileocæcal angle through which thrombi may travel without interfering with the nutrition of the bowel, as was illustrated by a later case reported by Sprengel in 1911. ' Wilms' operation ' had been performed for repeated daily rigors following appendicectomy

and drainage twenty-one days previously, and the patient developed a cæcal fistula and died later with multiple hepatic abscesses.

Braun's Operation.—Wishing to overcome the objections of Wilms' operation, Braun advised ligature of the ileocolic vein, which he claimed is not difficult to expose, is the only channel through which all emboli must pass to reach the liver from the appendix, and occlusion of which does not endanger the vitality of the bowel. His first attempt in 1907 was unsuccessful, but in 1913 he reported two successful cases in both of which the ileocolic vein was ligatured and several centimetres were resected. In one of these there was an enlarged tender liver and jaundice, showing that even in the presence of these later hepatic changes, if (as he claimed) the feeding focus in the vein below is removed in time, fatal pylephlebitis and liver abscesses may be prevented. Since this date there have appeared several communications in the German literature containing accounts of pylephlebitis complicating appendicitis treated by ligature of the ileocolic vein, a procedure which has become known as ' Braun's operation '. These cases may be divided into those in which ' primary ' ligature was performed during the first laparotomy in cases with pre-operative rigors, and those in which ' secondary ' ligature was performed at a subsequent laparotomy for repeated rigors following the original appendicectomy or drainage.

Primary Venous Ligature.—In *Table I* are collected the previously published cases in which the vein was ligatured at the time of the appendicectomy or drainage. No untoward complications, such as bowel infarction, appear to have followed the venous ligature in any of the cases, and nearly all these authors advocate tying the ileocolic vein in addition to appendicectomy or drainage in cases in which there is evidence of venous involvement as shown by rigors, or early hepatic involvement, or by visible thrombosis in the ileocolic vein or in the veins in the appendicular mesentery or around the cæcum.

A critical study of these cases, however, in spite of the fact that none of them subsequently developed pylephlebitis, shows that one must not too readily conclude that the course of the disease has been greatly altered by this extra interference.

Our discussion on rigors leads us to leave those cases with only one pre-operative rigor out of consideration. In those cases in which there was no thrombosis of the ileocolic cein or its radicles, it is difficult not to believe that the same result would have followed an adequate appendicectomy. Fromme's case was complicated by a large abscess in the transverse mesocolon, which was drained at the same time. Brutt's case had *B. coli* in the systemic blood-stream. Those cases in which rigors continued subsequent to the venous ligature for a long period, though recovery eventually ensued (e.g., Weil's case where rigors continued for three further weeks), are not very convincing. Two died of peritonitis.

Perhaps the most striking was the cessation of rigors and recovery in Sudeck's case of a girl aged 10, who had ten rigors after being ill for eight days with appendicitis. At laparotomy the superior mesenteric vein was found thrombosed and was ligatured proximal to the thrombus after exposure from below through the posterior layer of the transverse mesocolon. In some of the other cases also in which multiple pre-operative rigors had occurred and thrombophlebitis of the veins was found at operation (and jaundice and an enlarged liver in Braun's case) the subsequent cessation of rigors and recovery does suggest that the venous ligature did assist in preventing pylephlebitis from developing.

Table I.—PREVIOUSLY REPORTED CASES OF PRIMARY VENOUS LIGATURE

AUTHOR	PYÆMIC SYMPTOMS	FINDINGS AT LAPAROTOMY	PROCEDURE	RESULTS
Braun 1913	Rigors (several days). Jaundice. Enlarged liver	Appendix abscess. I.C.V. not thrombosed	Drainage. I.C.V. ligatured and 2 cm. resected	Recovery
Braun 1913	Rigors (8 days)	Appendix abscess. I. C. V. thrombosed	Drainage. 8 cm. of I.C.V. resected	Rigors for 4 days. Recovery
Weil 1920	Rigors (2 days)	Appendix abscess. I.C.V. obliterated	I.C.V. ligatured high up. Appendicectomy	Rigors for 3 weeks. Recovery in 10 weeks
Hempel 1923	Rigors (9 days)	I.C.V. palpable	I.C.V. ligatured. Appendicectomy	Further rigors. Recovered
Brunner 1918	Rigors (3 days)	Periphlebitis round I.C.V.	I.C.V. ligatured. Appendicectomy	No more rigors. Recovered
Fromme 1921	Rigors (1 month). Jaundice. Enlarged liver	I.C.V. thrombosed. Intraperitoneal abscess in transverse mesocolon	Abscess drained. I.C.V. ligatured	No more rigors. Recovered
Brutt 1921	Two rigors. *B. coli* in blood culture	Thickened I.C.V. Peritonitis	I.C.V. tied	Recovered
Braunig 1921	Three rigors	I.C.V. not thrombosed. Miliary abscesses in mesenteriolum	I.C.V. tied and resected. Drain	No more rigors. Recovered
Braunig 1921	One rigor	Appendicitis. I.C.V. dilated	Appendicectomy. I.C.V. resected	No more rigors. Recovered
Braunig 1921	Seven rigors	Gangrenous appendix. I.C.V. not thrombosed	Appendicectomy. I.C.V. ligatured	No more rigors. Recovered
Braunig 1921	One rigor	I.C.V. not thrombosed. Appendicitis	Appendicectomy. I.C.V. ligatured	No further rigors. Recovered
Braunig 1921	One rigor	Appendicitis. I.C.V. not thrombosed	Appendicectomy. I.C.V. tied	No more rigors. Recovered
Sudeck 1922	Ten rigors	Appendicitis. Superior mesenteric vein thrombosed	Superior mesenteric vein ligatured	One more rigor. Recovered
Hempel 1923	Rigors (10 days)	Thickened I.C.V. Peri-venous abscess	I.C.V. ligatured. Drained	No rigors. Died, peritonitis
Hempel 1923	Rigors (5 days)	I.C.V. filled with purulent thrombus	I.C.V. ligatured	Died, peritonitis

(I.C.V. = Ileocolic vein.)

The only certain conclusion that can be made regarding the prophylactic treatment of pylephlebitis is that early operation is of the greatest importance. A rigor in appendicitis should be considered just as urgent an indication for immediate laparotomy through a paramedian incision as the onset of peritonitis. There is also evidence that in cases of appendicitis giving a history of multiple pre-operative rigors, if there is visible thrombosis of the ileocolic vein or its small radicles in the cæcal area or early involvement of the liver, additional ligature of the ileocolic vein above the upper limit of the thrombus may assist in preventing an otherwise fatal pylephlebitis from developing. The ileocolic vein can easily be exposed by drawing the transverse colon upwards, the ascending colon to the right, and the small intestine to the left. It will be seen or felt as a thrombosed cord running from the cæcal angle upwards and to the left towards the corner made by the mesentery of the jejunum and the mesocolon (*see Fig.* 249). It is probably best to tie the vein before the appendicectomy. Venous ligature should not be attempted in those cases where circumstances are such that the procedure involves any serious risk of breaking down protective adhesions or spreading the infection in the peritoneum.

Secondary Venous Ligature.—Melchior in 1927 found the ileocolic vein thrombosed almost up to its opening into the superior mesenteric vein at a laparotomy two days after the onset of rigors thirteen days subsequent to an appendicectomy. He tied the vein immediately proximal to the thrombus and the patient recovered, two further rigors occurring five days later. Colp, Braunig, Melchior, Rëok, and Kleinschmidt have each reported a case where this operation has been carried out but without success. However, a careful study shows that in all the cases the ligature was applied after the rigors had been occurring for over a week, and in most of them nearer two weeks. This contrasts with Melchior's and our successful cases, where the thrombosed vein was ligatured within three days of the onset of rigors. It follows, therefore, that the operation, if it is to be performed at all, must be done very soon after the onset of pyæmic symptoms, before the infection has spread beyond the confines of the mesenteric veins.

Now a correct evaluation of the results of venous ligature at a second laparotomy for post-operative rigors is of the greatest difficulty, firstly owing to the great infrequency of the complication, and secondly owing to the lack of knowledge of the exact pathological condition present in those rare cases with similar symptoms which are treated conservatively and recover. Patients with rigors and signs of portal pyæmia after appendicectomy do undoubtedly occasionally recover without a further operation, and even a few well-authenticated cases of recovery from definite pylephlebitis have been described.

But from our study of the ominous significance of rigors and the prognosis of portal pyæmia complicating appendicitis and the dramatic cessation of rigors and recovery in Melchior's and our case following ligature of the vein proximal to the ascending thrombophlebitis, we feel, like many German observers, that this procedure is worth attempting provided it is carried out immediately after the onset of pyæmic symptoms. Post-operative pyrexia with the onset of rigors must be regarded as evidence of portal pyæmia, unless, of course, there are obvious signs of any such complication as pneumonia, pyelitis, cholecystitis, or subphrenic abscess. A second laparotomy should immediately be performed with a view

to ligaturing the ileocolic vein and preventing ascending pylephlebitis. Additional pain or tenderness ascending from the appendicular region, pain on pressure or enlargement of the liver, or jaundice only makes the indication for this prophylactic measure the more urgent. The ligature should preferably be applied to the upper part of the ileocolic vein, near to its junction with the superior mesenteric, well clear of the inflammatory area, where it can easily be identified (*see Fig.* 249). If the thrombophlebitis has already ascended beyond this point, as in our case, the superior mesenteric should be ligatured immediately proximal to the upper limit of the thrombus ; to reach this it may be necessary to follow the vein up by dissecting through the posterior layer of the transverse mesocolon. Ligature of the superior mesenteric vein about $\frac{3}{4}$ in. below its junction with the splenic vein was carried out in our case with success.

CASE REPORTS

REPORTS OF EIGHT CASES OF POST-OPERATIVE RIGORS COLLECTED FROM
5471 CASES OF APPENDICECTOMY

Case 1.—**Appendicectomy. Post-operative pyrexia and rigors. Non-hæmolytic streptococci in systemic blood. Mercurochrome injection into mesocolic vein. Recovery.**

E. T., male, aged 33, was admitted into the London Hospital complaining of pain in the right iliac fossa for one day. Operation by Mr. Donald : gangrenous appendix removed. Peritoneal cavity drained for three days. Remittent pyrexia followed and gradually increased, sometimes reaching 104° in the evening. On the seventeenth day a rigor occurred. Immediate laparotomy revealed a small abscess in the ileocæcal angle which was drained. Pyrexia continued and a further rigor occurred on the twentieth day and recurred almost daily. Blood culture on the twenty-fifth day grew non-hæmolytic streptococci. On the twenty-eighth day a third laparotomy was done through a mid-line incision ; 10 c.c. of 1 per cent mercurochrome were injected into one of the veins in the transverse mesocolon. The state of the liver, portal vein, or its tributaries and appendix could not be ascertained. Further rigors for three days only. Intermittent pyrexia continued and slowly decreased till it approached normal six weeks later. Slight pyrexia for three further weeks, and eleven weeks after the last operation the patient was discharged cured.

There were no signs of liver involvement in this case in spite of repeated rigors for fourteen days. Hæmolytic streptococci were grown from the systemic blood. There is no conclusive evidence that portal pyæmia caused the rigors in this case, and the relation of the appendicitis to the blood infection has been discussed in the text.

Case 2.—**Post-appendicular portal pyæmia. Two injections of mercurochrome into portal circulation. Death from multiple liver abscesses.**

A. T., male, aged 18, was admitted into the London Hospital with acute abdominal pain passing to the right iliac fossa which had started about twenty hours previously. Appendicectomy : gangrenous appendix and general peritonitis found. Two drainage tubes. High temperature followed, with onset of daily rigors on the second day. Laparotomy was performed on the seventh day. Liver abscess discovered : 12 c.c. of 2 per cent mercurochrome were injected into one of the veins in the transverse mesocolon. Drainage tube into Rutherford Morison's pouch. Temperature appeared to settle, but rigors recurred three days later (tenth day) and continued. A third laparotomy was done on the thirteenth day and 12 c.c. of 2 per cent mercurochrome were again injected into the portal system. The temperature became lower, but the patient eventually died six days later. Autopsy revealed multiple liver abscesses.

The development of the pylephlebitis was rapid in this case, a liver abscess being found at laparotomy on the seventh day. To hope for any possibility of success venous ligature would therefore have to have been carried out at a very early stage, probably when rigors were the only symptom. There is no note as to when enlargement or tenderness of the liver first appeared.

Case 3.—Appendicular abscess. Pre- and post-operative rigors. Portal pyæmia. Multiple liver abscesses. *B. coli* in systemic blood-stream. Multiple lung abscesses. Meningitis. Death.

H. D., male, aged 30, was admitted to the London Hospital with nine days' history of abdominal pain and vomiting, with onset of rigors three days previously. Tenderness in the right hypochondrium was present and the gall-bladder was thought to be palpable. A diagnosis of cholecystitis was made. Laparotomy was performed through a right upper paramedian incision. A high retrocæcal appendicular abscess was found displacing the gall-bladder. The abscess was drained. High pyrexia and rigors continued. *B. coli* was grown from the systemic blood in the later stages. At post-mortem ten weeks later multiple liver abscesses, multiple lung abscesses, a right empyema, and meningitis were found.

A 'primary' ligature of the mesenteric vein might have been attempted in this case, but on account of the position of the abscess the ligature would have to have been applied probably to the superior mesenteric vein to cut off all venous channels leading to the liver. The position of the abscess and the consequent adhesions might have rendered the operation extremely difficult or even impossible.

Case 4.—Appendix abscess. Appendicectomy. Post-operative pyrexia with one rigor. Recovery.

C. L., male, aged 32, was admitted to the London Hospital with one day's history of abdominal pain with a rigor. Appendicectomy and drainage. Intermittent temperature continued with one further rigor on the thirteenth day: 40 c.c. of 0·5 per cent mercurochrome were given intravenously. Pyrexia settled two weeks later. The patient was discharged cured.

No definite cause for the pyrexia and rigor was discovered in this case. No conclusive evidence of portal pyæmia.

Case 5.—Pelvic appendix abscess. Rigors and jaundice. Portal pyæmia. Liver abscesses. Death.

C. N., male, aged 38, was admitted into the London Hospital with twelve days' history of abdominal pain and shivering attacks. He was tender in the right hypochondrium and thought to be suffering from cholecystitis. Laparotomy : an appendix abscess in the pelvis with coils of small intestine and cæcum matted together was found. Drained. Jaundice, and rigors commencing on the third day followed. Death from pylephlebitis and liver abscesses.

Venous ligature is unlikely to have altered the course of the disease in this case as the patient had already been ill for twelve days, with rigors and a tender liver, before admission.

Case 6.—Gangrenous appendix. Post-operative pyrexia and rigors. Liver abscesses with secondary subphrenic abscess and right empyema. Death.

A. W., male, aged 37, was admitted into University College Hospital with abdominal pain and vomiting for twelve hours. Appendicectomy without drainage. Retrocæcal gangrenous appendix, not perforated. Low, irregular temperature followed, and daily rigors commenced on the fifteenth day. On the twenty-second day definite signs of consolidation were present at the base of the right lung. Leucocytosis (W.B.C. 14,000). Blood culture negative. Liver edge palpable and slightly tender. No jaundice. On the twenty-third day a transpleural search was made for a subphrenic abscess, with negative results. A laparotomy was therefore performed through a right upper paramedian incision. The liver was much enlarged and engorged. No pus was found. Irregular pyrexia continued with increasing weakness and delirium. The thoracic wound discharged seropurulent fluid which subsequently became thick green pus. The patient died after six weeks. Post-mortem revealed two large abscesses in the liver, one of which had burst through on the dorsal surface producing a subphrenic abscess : right empyema : pus in the pelvis.

Venous ligature might have been attempted in this case, though it would have to have been done at an early stage when rigors were the only symptoms and no other conclusive signs of portal pyæmia were present.

Case 7.—Gangrenous appendix. Pre- and post-operative rigors. Death.

A. H., male, aged 28, a native, was admitted into University College Hospital with two days' history of lower abdominal pain and one rigor. Appendicectomy: gangrenous appendix. High post-operative pyrexia with several rigors. The patient died on the fifth day. A limited post-mortem through the scar showed the local condition to be satisfactory. Thrombosis of the ileocolic vein.

Although complete post-mortem proof was unfortunately not available, the rigors, the absence of peritonitis, and the thrombosis of the ileocolic vein suggest strongly that the patient died of a gross infection of the portal system. As the ileocolic vein was not thrombosed at the original appendicectomy, it is unlikely that ligature of the ileocolic vein would have had any better result than adequate removal of the appendix.

Case 8.—Gangrenous appendix and peritonitis. Post-operative portal pyæmia and thrombophlebitis of the superior mesenteric vein. Ligature of the vein proximal to the thrombus. Recovery.

Female, aged 18. This case is, with the kind permission of Mr. Julian Taylor, reported in full in the text.

SUMMARY

1. A case is described of ascending mesenteric thrombophlebitis and portal pyæmia following appendicectomy. Infective thrombosis of the superior mesenteric vein with engorgement and swelling of the liver was found at a second laparotomy. The vein was ligatured proximal to the thrombus, with subsequent complete recovery.

2. The effects of occlusion of the mesenteric veins in man and experimental animals are reviewed. In man the superior mesenteric vein in the region of the transverse mesocolon, or its main branches, including the ileocolic vein, can be tied without producing infarction of the bowel, but occlusion of the small radicles distal to the anastomotic arcade may lead to intestinal necrosis.

3. The significance of rigors in typhlitis and the early symptomatology of portal pyæmia and pylephlebitis are discussed by reference to the literature and to eight original cases. Multiple pre-operative rigors and post-operative rigors are nearly always evidence of portal pyæmia.

4. Ligature of the upper part of the ileocolic and the superior mesenteric vein is discussed as a prophylactic measure against the development of pylephlebitis in cases of appendicitis with signs of portal pyæmia. The operation may be performed as a ' primary ' ligature at the time of appendicectomy in cases with pre-operative symptoms, and as a ' secondary ' ligature at a second laparotomy when portal pyæmia sets in subsequent to the original operation.

It gives me pleasure to conclude by expressing my sincere thanks for his kind permission to publish his case to Mr. Julian Taylor, whose great personal interest in the case inspired me to prepare this communication. I also wish to express my gratitude to those other members of the staff of the London and University College Hospitals to whom I am indebted for the use of the notes of their cases and for their kindly advice and criticism.

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INTESTINAL OBSTRUCTION BY GALL-STONES

By CECIL P. G. WAKELEY

SENIOR SURGEON, KING'S COLLEGE HOSPITAL, LONDON

AND F. WILFRED WILLWAY

SURGICAL REGISTRAR, KING'S COLLEGE HOSPITAL, LONDON

ACUTE mechanical obstruction of the bowel by a gall-stone is a well-recognized, though uncommon, entity. Undoubtedly most of the gall-stones which gain entrance to the intestinal tract are voided naturally. They cause no symptoms beyond those of the initial attack of biliary colic. Stones which are sufficiently large to cause intestinal obstruction never pass the whole length of the bile-duct, but enter the bowel by a process of ulceration. Such stones are usually more than an inch in diameter. Again, it is probable that a large number of stones which enter the bowel by this method are passed naturally per rectum (*Fig. 250*).

FIG. 250.—This stone was passed naturally by a woman aged 56 years. She gave a history of epigastric pain and flatulence for ten years. She had also had some acute attacks of biliary colic, but had never been jaundiced. It is a pure cholesterin stone and is soapy to touch. The eroded end suggests it had projected for some time into the duodenum and had been eroded by the acid chyme (*Natural size.*)

Some recent figures of the frequency of this condition in relation to the other causes of intestinal obstruction are given later. Earlier accounts of its frequency when causing symptoms place the occurrence rather higher than the recent statistics quoted.

It is interesting to speculate whether the condition is on the decrease in view of the popularity of cholecystectomy at the present time. Alternatively, other forms of obstruction may be on the increase. Owing to the tremendously increased number of abdominal operations performed, it might be supposed that intestinal obstruction by bands would be increasing in frequency, and thus reduce the relative proportion of other causes. This is not borne out by the two symposia quoted below. In 1920–5 the frequency of obstruction by bands was 20 per cent of all causes, while in 1925–30 it was 14 per cent. In 1884 Treves wrote: "An examination of the London Hospital records [of obstruction] shows that cases ascribed to fæcal accumulation are the most numerous, then come cases of stricture of the large intestine, then intussussception, and next in order of frequency, strangulation by bands. Obstruction due to tumours of the bowel ranks next, then follows the blocking of the gut by gall-stones or foreign bodies, while the remaining forms of intestinal obstruction may be spoken of as rare." It is interesting to note that Treves ranks highest intestinal obstruction by fæcal impaction,

whereas in the 1932 review this cause accounted for 17 cases only, i.e., 0·47 per cent. Obstruction by gall-stones is not likely to become very infrequent, as numbers of symptomless cases of gall-stones in the gall-bladder may be discovered at routine autopsies. In such cases there is always the possibility of symptomless ulceration with subsequent obstruction. (*Tables I and II.*)

Table I.—Recent Statistics

AUTHORITY	CASES OF GALL-STONE OBSTRUCTION	TOTAL CASES OF OBSTRUCTION	PERCENTAGE FREQUENCY
Vick. (Symposium on Intestinal Obstruction 1932)	47	3625	1·3
Souttar. (Symposium on Intestinal Obstruction 1925)	28	1655	1·7
Meyer and Spivack (1934)	2	505	0·4

Table II.—Earlier Statistics

AUTHORITY	CASES OF GALL-STONE OBSTRUCTION	TOTAL CASES OF OBSTRUCTION	PERCENTAGE FREQUENCY
Osler (1900)	23	295	7·8
Leichtenstern	41	1152	3·5
Barnard (1902)	8	360	2·2

SOME POINTS OF SPECIAL INTEREST FROM EARLIER RECORDS

Associated Volvulus.—A gall-stone in the small intestine can excite such vigorous contractions that a volvulus may follow. Mayo-Robson operated on two such cases successfully. It must, however, be an extremely rare phenomenon.

Spontaneous Relief.—A gall-stone after causing obstruction may become free and be voided naturally. This has occurred in a number of cases, but not always with recovery, as a number of patients, after passing the stones, have collapsed and died. A case is mentioned by Treves of a woman of 63 who, after five days of complete obstruction, became relieved and later passed a stone more than an inch in diameter. This patient had an irreducible hernia containing bowel through which the stone must incidentally have passed. The relief experienced in this case was probably due to the stone passing into the cæcum. In another case the stone impacted in a loop of bowel in a hernia, and then ulcerated through the skin.

SUMMARY OF ELEVEN CASES SUBJECTED TO OPERATION

We have been able to review a series of cases subjected to operation, and secure specimens from other cases which, for various reasons, were not referred to a surgeon. A full account of these cases is given on pp. 388–93, but a summary of their main features is convenient at this stage. (*Table III.*)

The only recent comparable series of cases we can find is that of Professor Grey Turner, who in 1927 published a review of eight cases. It is valuable to compare our figures with his, and this has been done throughout the following paragraphs. The earlier literature abounds with records of cases noted as interesting, but few record a definite series of cases. In some of the recorded series cases which were not subjected to operation are confused with those which were, and this rather obscures the issues. In 1910 Sherren edited H. L. Barnard's notes on this condition, with Barnard's series of six personal cases and eight other collected cases. Barnard's article is classic, and should be read by all who are interested in this subject. Some of the earlier cases reported make very interesting reading, and the clinical features are often bizarre. The impression is received that patients in those days were of sterner stuff, when one reads of their recovering from operation on the eighth day of absolute obstruction!

COMMENTARY ON CASES IN THIS SERIES

Age.—The average age of the patients in our series is 66 years, the extremes being 81 years and 44 years. Only three cases were under 60 years of age. In Grey Turner's series the average was 67 years, with extremes of 79 and 56. In his report, however, he refers to a very interesting case of a youth, who, during the seven years between 18 and 25, voided per rectum eight gall-stones, two of which were sufficiently large to require removal with forceps. Subsequently the patient did well. Schuller collected 119 cases; his age limits were 18 and 94 years.

Sex.—It is remarkable that in this series all 11 cases were female. Of Grey Turner's 8 cases, only 1 was male. This gives a combined ratio of 18 to 1, or only approximately 5 per cent of male cases. It is well recognized that gall-stones are commoner in the female sex in any case, but the usual ratios given are 2 or 3 to 1. The earlier writers record male cases more frequently, and Barnard gives the ratio as 4 to 1, or 25 per cent of male cases. He further states that this agrees with the relative frequency of stones in the gall-bladder.

Mortality.—In our series the mortality was 3 out of 11 cases, i.e., 27 per cent. Grey Turner's series showed a mortality of 2 out of 8 cases, i.e., 25 per cent. The mortality of the British Medical Association series in 1925–30 was 70 per cent, while in the 1920–5 series it was 50 per cent. The two cases quoted by Meyer and Spivack both died. The seriousness of the condition is, in our opinion, due to two main factors :—

1. The type of patient in whom the condition occurs. These elderly patients are poor subjects for operation. Some are very obese subjects, while in others, wasting was noted. In two cases—one fatal—sugar was observed to be present in the urine.

2. Operation is not infrequently delayed in these cases, because the obstruction tends to be intermittent. The approximate period of duration of symptoms

Table III.—Summary of Eleven Cases Subjected to Operation

Case No.	Age and Sex	Termination	Approximate Time before Operation	Pre-operative Diagnosis	Whether Symptoms Intermittent	Previous History	Site of Impaction	Whether Possible to Dislodge the Stone at Operation
1	76 F.	Recovered	18 hours	Intestinal obstruction. ? cause	No	Vague	Ileal loop in pelvis	Stone pushed back into healthy bowel and then removed
2	75 F.	Recovered	4½ days	Intestinal obstruction. ? cause	Marked	Definite history	Lower end of small intestine	Stone pushed back into healthy bowel and then removed.
3	55 F.	Died	? 14 days	Intestinal obstruction. ? cause	Not noted	Constipation	4 in. from ileo-cæcal valve	No note *re* attempt at dislodgement
4	71 F.	Recovered (Stormy convalescence)	6 hours	Carcinoma of colon	Not noted	Long history	Terminal ileum	Stone could not be dislodged ; removed by direct incision
5	62 F.	Recovered	4 days	Intestinal obstruction. ? cause	Not noted	Definite history	Lower part of ileum	Stone could not be dislodged ; removed by direct incision
6	71 F.	Recovered	Not ascertained	Intestinal obstruction. By a band	No	Not noted	Middle of ileum	Stone was pushed on into a healthy portion of bowel and removed
7	65 F.	Died	48 hours	Intestinal obstruction. ? cause	Yes	Noted as absent	7 in. from duodenal-jejunal flexure	Stone was pushed on into a healthy portion of bowel and removed
8	57 F.	Recovered	20 hours	Gall-stone obstruction	Yes	Definite history	Middle of small gut	Stone was pushed back into healthy bowel and removed
9	73 F.	Recovered	Less than 12 hours	Intestinal obstruction. ? cause	No	Absent	5 in. from ileocecal valve	Stone could not be dislodged ; removed by direct incision
10	44 F.	Recovered	Not ascertained	Gall-stone obstruction	Yes	Definite history	8 in. from ileo-cæcal valve	Stone pushed back with difficulty into healthy bowel and then removed
11	81 F.	Died	36 hours	Carcinoma of sigmoid	No	Vague	Terminal ileum	Stone could not be dislodged ; removed by direct incision

is listed in the main table. It is impossible, however, to be certain when obstruction became absolute. It will be noticed to be extremely variable.

In the fatal cases in our series it may be noted that :—

One, aged 81 years, was obstructed for 36 hours. She lived 8 days after the operation, developed a fæcal fistula, and died with symptoms of uræmia and ileus.

One, aged 65 years, was obstructed for 48 hours. In this case the obstruction was very high (upper jejunum). She lived for 9 days after the operation.

One, aged 55 years, had intermittent symptoms for 14 days. This patient had a double obstruction. (This will be alluded to later.)

Previous History Suggesting Cholelithiasis.—Four cases of the 11 listed here had a definite gall-bladder symptomatology. In some cases this extended over years. Two others had more indefinite symptoms such as dyspepsia or indigestion, and are listed as ' vague '. In the other 5 no special abdominal symptoms were present and there was little reason to incriminate the gall-bladder. In only 2 cases (18 per cent) was a pre-operative diagnosis of gall-stone obstruction made. One of these had had an attack of jaundice three weeks previously. The cases were subjected to operation because of intestinal obstruction, a common pre-operative diagnosis being carcinoma of the colon. In one case a mass, the impacted stone, was felt in the left iliac fossa and was taken to be a growth in the sigmoid loop.

Site of Impaction of the Stone.—Courvoisier's figures for a series of 53 cases examined at autopsy, are as follows :—

Impacted in the duodenum : 22·2 per cent.
Impacted in the ileum : 65·4 per cent.
Impacted at the ileocæcal junction : 10·0 per cent
Impacted in the sigmoid loop : 2·4 per cent.

In Mr. Grey Turner's series :—

Impacted in small intestine : 87·5 per cent.
Impacted in pelvic colon : 12·5 per cent.

He also separately records a case of obstruction of the transverse colon by a giant gall-stone

All 11 cases in our series had stones impacted in the small bowel—one patient also having a stone impacted in the rectum ; the sites being divisible as follows (the apparent twelfth case is due to one case being one of double obstruction) :—

Upper jejunum : 1 = 8·5 per cent.
Middle of small intestine : 1 = 8·5 per cent.
Middle of ileum : 2 = 17 per cent.
Lower end of ileum : 7 = 57·5 per cent.
Rectum : 1 = 8·5 per cent.

In the cases of fistula we investigated, there is one of duodenal obstruction by fibrosis following a fistula, but we have never seen a stone impacted in the duodenum, although Courvoisier noted 7 cases.

Mode of Ulceration.—It is not always possible, and indeed it is doubtful how far it is desirable, to attempt at operation to decide how the stone gained access to the intestine. At laparotomy a hand was passed up to the gall-bladder region in 5 of our cases : in 4 of these dense adhesions were felt, and it was presumed that a cysto-duodenal fistula was present ; in the other case the gall-bladder appeared to be perfectly normal, and the stone is presumed to have ulcerated through the common bile-duct. It is interesting to note that this was not the

case which presented the previous symptom of jaundice. In 2 further cases there was post-mortem proof that a cysto-duodenal fistula was present. This makes an aggregate of 6 cases of cysto-duodenal ulceration to 1 of common-duct ulceration. In the other 4 cases it is impossible to be certain what form of fistula was present.

Possibility of Dislodging the Stone.—The usual text-book description of this condition concludes with advice that the stone should be moved to a healthy part of the bowel before the gut-wall is opened. We have attempted this in all our cases, but with only partial success. It would obviously be more satisfactory to open the collapsed and relatively healthy part of the bowel distal to the obstruction, than the distended, hyperæmic, proximal portion, and either of these sites is preferable to the actual site of impaction. If the site of impaction is gangrenous it would be best to open this portion and exteriorize the affected part, these patients being too ill to stand resection. Our experience was as follows :—

> In 2 cases the stone was successfully pushed on.
> In 4 cases the stone could not be pushed on, but was pushed back. (In one with considerable difficulty.)
> In 4 cases the stone could not be dislodged at all.
> In 1 case no note of the result of this manœuvre was made.

FIG. 251.—*Case* 11. Stone removed from the patient. It is rather more than 2 × 1 × 1 in When dry it weighed 210 gr. It readily broke into two stones, which have been cemented together by layers of bile pigments. (*Natural size*)

These findings are usefully compared with the actual cause of the obstruction which is almost certainly spasm of the bowel.

More than One Stone Causing Obstruction.—Double simultaneous obstruction must be exceedingly uncommon, but yet is liable to occur. *Fig.* 251 shows the type of stone which, should it fragment, is liable to produce such double obstruction.

Case 3 is an instructive example. Here the first stone was impacted in the rectum. It was removed, with temporary improvement. Signs of obstruction recurred eighteen hours later, and at laparotomy a second stone was found causing obstruction in the terminal ileum (*Fig.* 252). It can be seen that these stones fit together and so arranged would resemble *Fig.* 251, the stone removed whole from *Case* 11. If this latter stone had broken, double obstruction might readily have occurred. Drew records a patient of 70 in whom two stones were impacted in the upper jejunum at some distance from each other, the second

FIG. 252.—*Case* 3. Stones removed from the patient. The larger stone was impacted in the ileum, while the smaller was wedged in the rectum. The latter was removed digitally. (*Natural size*)

stone being only found on routine exploration after the first had been removed. The impaction was 18 in. from the flexure. The lower stone did not appear to be causing obstruction, but on the other hand was so tightly wedged that it had to be removed through a separate incision. This case also presented the peculiarity of cystic pneumatosis. It was, unfortunately, fatal, but it should be noted that the obstruction was high. The practical point thus arises that in every case a search should be made for a second stone obstructing, especially if the first removed appears faceted. *Fig.* 250 shows a stone which a patient brought in her hand to hospital, having successfully passed it. It again gives the appearance of two stones joined together. This patient's subsequent history was uneventful.

THE MODE OF PRODUCTION OF BILIARY FISTULÆ

The gall-bladder appears to have a natural aptitude for becoming adherent to structures in its vicinity. The stones in its cavity lead to a pressure necrosis of its wall, doubtless accompanied by a low-grade infection, and in this way a fistula is formed. These fistulæ are most frequently into the duodenum, though they have been described as occurring between the gall-bladder and stomach, colon, renal tract, or even uterus or vagina, while rarely the stones may discharge by a sinus in the anterior abdominal wall. Occasionally, encysted collections of gall-stones are found in the peritoneal cavity. In one rare case a fistula between the liver and lung has been reported, the patient coughing up bile in the sputum.

Courvoisier gives the following result in 36 autopsies on cases of intestinal obstruction by gall-stones :—

	CASES
Fistula to duodenum	25
Fistula to ileum	1
Fistula to colon	1
Fistula to colon and duodenum	2
No fistula	7

Treves is very sceptical as to whether a stone of sufficient size to cause intestinal symptoms can pass via the common bile-duct. He mentions Abercrombie as recording a case in 1837, but throws doubt on this case as the gall-bladder was stated to be " in a state

FIG. 253.—The drawing shows the second part of the duodenum opened on the border opposite the entrance of the common bile and pancreatic duct. A stone can be seen impacted in the common bile-duct and beginning to ulcerate through into the duodenum. This stone was ? × ½ in. and could cause intestinal obstruction. A, Commencing ulceration; B, Ampulla of Vater. (The viscera illustrated in *Fig.* 254 are from the same case as this specimen.)

of inflammation and was softened and partially disorganised ".

Figs. 253 and 254 are interesting in this respect as showing the beginnings of a fistula where the stone would be of sufficient size to cause obstruction. Here the fistula is between the common bile-duct and the duodenum. This offers a possible solution to the apparent impossibility of a stone large enough to cause obstruction passing the papilla of Vater. The story

of this case is truly remarkable.   The specimens came from a man who died from
severe burns while on his way to hospital.   He had been smoking his pipe in a
feather bed when he inadver-
tently fell asleep.   The pipe
slipped from his mouth and
ignited his bedding.   Autopsy
showed a cirrhotic liver with
obstructive jaundice, a gall-
bladder which was full of stones
and its wall fibrotic, and a stone
impacted in the common bile-
duct and about to ulcerate into
the duodenum—an extraordin-
ary museum of pathological
derangements, and a good
example of the ˍoccasional re-
wards of routine autopsies.

Multiple fistulæ must be very
uncommon, though cases have
been reported where the viscus
has communicated with the
duodenum and colon at the same
time.   In one case in our series
(*Case* 3) autopsy showed two
fistulous communications about
1 cm. apart; the upper one
small, the lower large and ragged.
The stones removed are shown
in *Fig.* 252.   It was thought
at the time that the smaller
rounded   stone   had   passed
through the upper opening and
the large irregular stone through
the lower ragged opening.

FIG. 254.—This specimen from the same case as
Fig. 253 shows the liver and biliary apparatus.   The gall-
bladder wall shows marked fibrosis and the gall-bladder
was full of stones.   The dilated biliary ducts are well
shown.   A, Site of obstruction of the stone in the common
bile-duct;   B, Common bile-duct;   C, Common hepatic
duct;   D, Orifice of hepatic duct;   E, Dilated cystic duct.

Figs. 255 and 256 show an extremely interesting specimen where the duodenum
was obstructed by cicatrization after the establishment of a cysto-duodenal fistula.
This patient, aged 71 years, complained of attacks of vomiting of three weeks'
duration.   The vomiting was of a very severe nature and unaffected by any diet
or alkalis.   She had no other symptoms and her previous history was normal,
except for an attack of food poisoning nine months previously (the significance
of which will be discussed later).   A barium meal which showed constant narrow-
ing in the region of the pylorus, with much stenosis and twenty-four hours'
residue, had been taken previously.   The patient was very wasted and in poor
condition.   She was admitted to hospital to prepare her for laparotomy, but she
sank into coma and died.   The illustrations show a large fistulous communication,
1 in. across, between the gall-bladder and duodenum.   The duodenal wall opposite
the fistula was much scarred and contracted.   A stone (*Fig.* 255—inset), lay in
the fistula.   This measured $\frac{7}{8}$ in. in most diameters and round it were packed

(*Natural size.*)
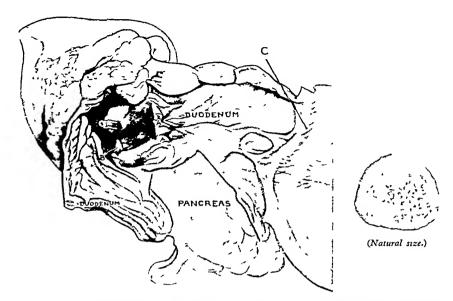
FIG 255 —The specimen illustrates duodenal obstruction by scar tissue following a cholecyst-duodenal fistula *Fig.* 256 is from the same case. The duodenum has been opened opposite the fistula A and B denote the marked scar ridges which actually led to the obstruction; C, Pylorus The glass rod is the same as that shown in *Fig.* 256 and shows the fistulous opening. The recess was occupied by the large stone shown alongside, and six smaller ones not illustrated. The condition is virtually one of hour-glass gall-bladder
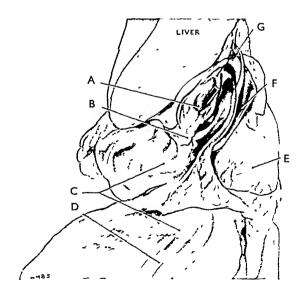
FIG 256 —This drawing illustrates the other half of the hour-glass gall-bladder shown in *Fig* 255 The glass rod illustrated is the same as that in *Fig.* 255. It leads from the two parts of the gall-bladder into the duodenum A, Gall-bladder, B, Adhesions between gall-bladder and duodenum, C, Duodenum (posterior aspect), D, Pylorus, E, Pancreas, F, Common bile-duct, G, Hepatic duct.

several other stones, not illustrated. The duodenal obstruction must have been almost complete. It is probable that the attack of 'food poisoning' nine months previously represented the establishment of the fistula, the subsequent cicatrization leading to the stenosis. It is interesting to consider the symptomatology of the ordinary case with this autopsy finding in mind. The early symptoms are often vomiting, pain, and collapse, the vomitus being gastric contents or bile-stained fluid. This passes off and the patient improves, vomiting recurring later, however, and this time of intestinal contents—the so-called 'fæcal' vomiting. It is reasonable to suppose that the first bout of vomiting is due to the stone entering the duodenum, the intermission being associated with its dislodgement, and the final symptoms being due to its impaction elsewhere. This constitutes the classical story. The obstructing stone itself, as pointed out by Barnard, may often have a narrow nipple-like end composed of pure cholesterin. The pigment layer which would normally cover this was washed away by the chyme while the stone projected into the duodenum. *Fig.* 250, showing a stone which was successfully passed per rectum, demonstrates this erosion.

The Subsequent Fate of the Bi-mucosal Fistula.—After the stone, or stones, have been successfully extruded into the intestine, the fistula begins to contract. This is probably a rapid procedure. Its exact time is difficult to estimate, as the period of delay of the stone in the intestine is very variable. In the autopsies we have seen, the fistula is always far smaller than the stone which passed through it, though the material was examined within a fortnight of the first occurrence of intestinal obstruction. There are cases, however, reported by Grey Turner and others, where, at autopsy, the stone could be returned through the fistula into the gall-bladder. These cases are uncommon, and it is usual to find the fistulous orifice much contracted. *Figs.* 257 and 258 show the typical findings. In this case the stone weighed, when dry, 216 gr., while the fistulous opening is less than $\frac{1}{2}$ in. in diameter. This patient died nine days after the commencement of symptoms. It is thus established that the fistula contracted considerably. The final result is a matter for conjecture. Grey Turner states that it never completely closes, and cites in support of this opinion cases where at the operation of cholecystectomy he has found infundibuliform communications between the gall-bladder and duodenum. He points out the danger of regarding such communications as adhesions, when in actuality they connect with the bowel. Such an end to the condition must be less usual in our experience than for the gall-bladder to shrivel up almost completely. This is illustrated well by *Figs.* 256–259. It may be stated that cholecystectomy should never be undertaken following recovery from intestinal obstruction by a gall-stone.

The Obstructing Stone.—We have earlier pointed out that these stones may be double. The time the stone may spend in the intestine is of interest. The contents of the stomach usually take from four to six hours to traverse the small intestine; we have no reason to believe that once the stone is free it takes any longer. The stone may, however, project into the intestine for some period before it is dislodged. This probably accounts for the wide variations in some of the older accounts in which the establishment of the fistula was confused with the entrance of the stone into the intestine. The illustration from Professor Grey Turner (*Fig.* 259) shows that this may be a lengthy business. Sir Thomas Smith reported a case where the stone was thought to have resided in the intestine for
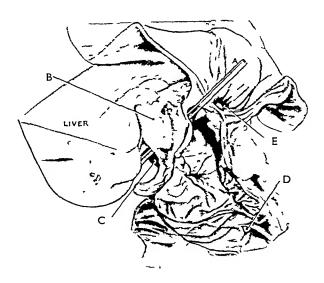
FIG 257 —*Case* 11 The specimen shows a typical cholecyst-duodenal fistula. The glass rod (A) is the same as the rod A in *Fig* 258 It passes through the fistula B, Adhesion, C, Gall-bladder, D, Ampulla of Vater, E, Pylorus
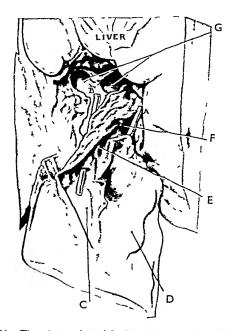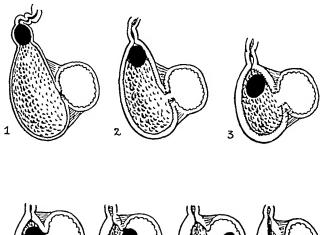
FIG 258 —*Case* 11 The glass rod A (cf *Fig* 257) is in the fistulous opening between the gall-bladder and duodenum The rod B is passing down the common hepatic duct The adhesions between the shrunken gall-bladder and the duodenum are well shown C, Dilated common bile-duct, D, Duodenum, E, Cystic duct, F, Remains of gall bladder, G, Hepatic duct

fifteen years. F. S. Eve considered that in one of his cases the stone was in the bowel ten years before obstruction occurred.

It is unusual for the stone to gain accretions while in the intestine. Dr. Charles Newman has kindly assayed the stones of this nature in King's College Hospital Museum, and reports a complete absence of fæcal accretion. Treves, however,
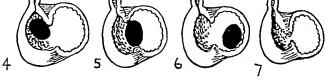
FIG. f259.—A series of diagrams showing how gall-stones may find their way into hollow viscera 1, A calculus is impacted in the neck of an inflamed and distended gall-bladder which has become adherent to the neighbouring bowel; 2, The gall-bladder has ulcerated into the intestine; 3, The gall-bladder drains freely into the intestine, and, tension being relieved, it begins to contract; 4, The process of contraction, which is partly due to the development of scar tissue, continues and the calculus is pressed against the opening in the bowel; 5 and 6, Show the transit of the calculus into the bowel, 7, The calculus has travelled on down the intestine, the fistula contracts, and the gall-bladder continues to shrivel. (*After Grey Turner, modified*)

reported a case where a calculus removed from the intestine was composed of a nucleus of a small gall-stone covered in layers by fæcal matter and magnesium carbonate. The stone measured $1\frac{1}{2}$ in. and the patient had been in the habit of taking magnesia for years.

CASE REPORTS

Case 1.—Mrs. Stella J., aged 76, had always enjoyed good health and had brought up a family of four girls and three boys. She was a large woman of 14 stone in weight, but she had led an active life and played golf up to the age of 65. In June, 1919, she first noticed that she had some indigestion after food, but she paid no attention to this. She noticed also that she was inclined to be somewhat constipated, which was not usual for her. On the evening of July 5, at 8 p.m., she was seized with acute abdominal pain, and shortly after this she vomited. Her doctor was called, and as he could not find any definite area of tenderness, he gave her an injection of morphia which eased the pain until 2 a.m. on July 6, when the vomiting and pain returned.

The maximum pain seemed to be situated in the region of the umbilicus. Her doctor saw her at 9 a.m. on July 6 and found that the abdomen was distended, the pulse-rate was 110, and the temperature normal. *The patient was sweating and looked ill; she was* vomiting about every four hours, and the vomit was beginning to become fæcal in character.

The patient was admitted to a nursing home and an operation was performed at 2 p.m. on July 6. Just prior to operation the stomach was washed out. Gas and oxygen anæsthesia was given, and the abdomen was opened by a right paramedian incision. As soon as the peritoneum was incised, a considerable amount of blood-stained fluid escaped. The small intestine appeared very much distended, and by introducing a finger into the abdominal cavity a hard mass was felt in a loop of small intestine which was situated in the pelvis. The loop of gut was delivered outside the abdominal cavity, and with care the impacted gall-stone was gently milked backwards for several inches into the dilated ileum. An incision was made into the antimesenteric border of the gut over the stone, and the stone was removed. The opening in the gut was sutured by means of a double row of sutures and the gut returned to the abdomen. The liver and gall-bladder were palpated, but no other gall-stones could be felt. The abdominal wall was closed in layers. The patient vomited twice after the operation, but made an uninterrupted recovery.

In this case operation was carried out early and the patient was in good condition in spite of the fact that her doctor gave her ¼ gr. of morphia after the obstruction had become absolute.

Case 2.—E. W., female, aged 75, was seen on Feb. 1, 1923, complaining of abdominal pain and vomiting. She gave a history of fæcal vomiting with abdominal colic and absolute constipation for three days; there was an indefinite history of chronic indigestion, culminating on one occasion with a similar attack thought to be due to gall-stones. On examination the abdomen was distended and the temperature subnormal. She was kept under observation. The bowels were absolutely confined, but there was much less pain and no vomiting. Thirty-six hours later the patient began to vomit material which was definitely fæcal in character; operation was then decided upon.

A median laparotomy was performed. As soon as the peritoneal cavity was opened, distended small intestine protruded through the wound. A large gall-stone, subsequently found to weigh just under ½ oz., was felt in the lower end of the small intestine. The stone was closely held by a ring of spasmodic contraction of the gut; above this the intestine was greatly distended, whilst below it was emptied and narrowed. The stone was pushed up the intestine for a short distance and then removed, and the opening of the gut was closed by two layers of sutures. The patient made an excellent recovery.

This case is interesting in that the obstruction was not absolutely typical in its manifestations. The fæcal vomiting was intermittent, and the pain only severe when the vomiting was present. These facts, together with the actual finding of a ring of spasm gripping the stone, suggest that the intermission was due to the stone passing on for a distance, becoming held up, and then passing on again.

Case 3.—M. T., female, aged 55, was admitted to hospital on March 29, 1923, suffering from intestinal obstruction. The patient stated that she had been well most of her life, but had suffered from occasional 'giddy' attacks during the last fifteen years. She had had almost complete constipation for a fortnight. She stated that she was always constipated, but never as bad as this. On examination the patient was found to be large and fat, with an unhealthy complexion. The skin was moist and cold. The bowels were absolutely confined; the abdominal wall was so fat that palpation was difficult; however, there was marked resonance on percussion, general tenderness, but no rigidity. A soap enema was given with a small result, and the passage of a little flatus. On examining the rectum a large gall-stone was discovered, too large to be passed naturally, and so it was removed digitally. The obstructive signs abated temporarily, and flatus was passed. However, eighteen hours later fæcal vomiting recommenced with abdominal pain. Operation was decided upon.

A mid-line laparotomy was performed, and a large gall-stone, considerably bigger than the one which was removed from the rectum, was found impacted in the lower end of the ileum, about 4 ft. from the ileocæcal valve. There was great distension of the small intestine. The stone was removed, and the intestine closed by two layers of sutures. It was found necessary to puncture the gut with a trocar and cannula before it could be replaced; the puncture was closed by means of a purse-string suture. The patient rallied after twenty-four hours, but died three days after the operation from paralytic ileus.

At autopsy well-marked paralytic ileus was present. The gall-bladder was firmly

adherent to the first part of the duodenum.   On opening the duodenum two fistulous communications with the gall-bladder were found about 1 cm. apart.   The upper one was smaller, and in all probability the stone which was removed from the rectum had ulcerated its way through it.   The lower aperture was large and ragged, and the bigger stone must have forced its way through it.   The two gall-stones are shown in *Fig.* 252.

Case 4.—Mrs. Mabel H., aged 71, had enjoyed good health up to the age of 50, when her periods stopped.   She was the mother of two girls and a boy, and she had always worked hard in her house and spent a lot of time·in her garden and looking after an extensive rock garden entirely by herself.   When her periods ceased at the age of 50, she began to have abdominal pain and was jaundiced on three occasions.   She visited several continental spas, and underwent many forms of treatment, both at home and abroad, but she did not get any permanent relief.   At the age of 60 she was treated for neurosis and enteroptosis and given an abdominal belt.   Her appetite became very poor and she began to lose weight.   A barium meal did not reveal anything abnormal in the gastro-intestinal tract.   About this time she went to live at Brighton and continued in somewhat poor health until the age of 70, when she returned to London in May, 1926.   She said she felt better and began to put on weight until Dec. 6, two days after her 71st birthday, when she was seized with violent abdominal pain at 4 p.m.   The pain doubled her up and soon afterwards she vomited.   Her doctor visited her two hours later and diagnosed intestinal obstruction due to a growth in the colon, and she was admitted to a nursing home.   Vomiting persisted and visible peristalsis was seen on more than one occasion.   The abdominal distension was not very marked.   Rectal examination was negative.

At 10 p.m., on Dec. 6, under spinal anæsthesia, the abdomen was opened by a right paramedian incision; coils of dilated small intestine were discovered, and in the terminal ileum a hard mass was found.   The loop of gut was delivered, and an attempt was made to dislodge the stone into the gut above, but this was found to be impossible, so an incision was made over the stone and it was removed.   The small intestine was sutured by a double layer of sutures, and the abdominal wound closed in layers.   Convalescence was stormy; the patient developed bronchitis and her bowels were only persuaded to act by giving ox-bile enemata every second day.   However, she was able to leave the nursing home just twenty days after the operation.

Case 5.—E. W., aged 62 years, a married woman, was taken ill with abdominal pain and vomiting on March 31, 1928.   This persisted for four days, when she was seen in consultation and admitted to hospital as an urgent case on April 4.   She presented the typical appearance of intestinal obstruction.   The temperature was 97°, pulse-rate 100, respirations 20.

FIG. 250.—*Case 5.*   Stone removed from patient.   (*Natural size.*

The abdomen was distended and tympanitic.   Visible peristalsis was noted.   Her urine contained sugar (she was later proved to be a mild diabetic).   Her past history revealed numerous attacks of pain in the right hypochondrium.

Laparotomy was urgently performed on April 4.   The abdomen was opened through a right lower paramedian incision.   A gall-stone was found impacted in the last loop of the ileum.   It could not be dislodged and was removed by direct incision (*Fig.* 260).   A tube

was stitched in to drain the bowel. The upper abdomen was examined and further stones were palpated in the gall-bladder, which was very adherent. The patient made an excellent recovery. The enterostomy closed normally at the end of a fortnight.

Case 6.—S. S., female, aged 71, was admitted to hospital on June 13, 1928. On admission the patient had all the symptoms of acute intestinal obstruction, and was vomiting upper small intestinal contents. There was distension in the upper part of the abdomen, and intermittent colicky pain. No history as regards the investigation of the gall-bladder was taken.

Operation was performed under chloroform and ether anæsthesia. The abdomen was opened through a rectus slide-out incision on the right side below the umbilicus, as a pre-operative diagnosis of small-intestine obstruction, probably by a band, had been made. When the peritoneum was opened there was some free fluid, which was clear. A hand was inserted, and immediately found, about the middle of the ileum, an impacted gall-stone the size of a pigeon's egg. The loop of bowel was then delivered, and clamps were applied above and below the stone. The stone was pushed downwards in the bowel until it reached a healthy portion. The bowel was incised longitudinally, and the stone removed. The hole in the bowel was closed transversely and the abdomen was closed in layers. The operation lasted ten minutes. The patient made an uninterrupted recovery and left the hospital fourteen days after the operation.

Case 7.—P. S., female, aged 65, was admitted to hospital on Nov. 13, 1928. On admission the patient complained of abdominal pain and vomiting of two days' duration. For the previous two days the patient had had intermittent abdominal pain with vomiting. The bowels had not moved for five days. She had always been constipated, but there had been no previous similar attack. She had no urinary trouble. She vomited brown fluid and had passed no flatus per rectum.

On examination the patient had an extremely toxic look. The tongue was dry and furred; the abdomen was distended, tender, and tympanitic, especially under the right costal margin. There was no marked pain. An enema was given with no result. The urine showed a slight trace of sugar.

Operation was performed under gas, oxygen, and ether anæsthesia. A pre-operative diagnosis of acute intestinal obstruction of unknown causation had been made. A rectus slide-out incision was made on the right side, and an exploration carried out. There was much free clear fluid in the peritoneal cavity. The bowel seemed collapsed everywhere. A markedly congested cæcum and appendix were delivered, but no active disease was found. The gall-bladder was found buried in omental adhesions. A gall-stone the size of a pigeon's egg was found impacted in the upper jejunum about 7 in. beyond the junction of the duodenum and the jejunum. This was pushed along into the healthy gut, removed, and the wound in the intestinal wall was sutured. The abdominal wall was closed in layers.

The patient seemed to recover from the immediate operation, and treatment was commenced for her diabetes. She slowly went downhill and died nine days after the operation from hypostatic pneumonia.

Case 8.—Fanny C., aged 57, was admitted to hospital on June 6, 1929. On the afternoon of admission the patient was suddenly seized with intense pain in the right hypochondrium and in the right shoulder. Similar attacks had occurred on several previous occasions. She was sent into hospital as a case of acute cholecystitis. She had vomited stomach contents on two occasions. She was kept under observation, the presumed diagnosis being acute cholecystitis. During the night she vomited again and complained of intermittent colicky pain, still thought to be biliary in origin. Morphia and atropine were administered, and the patient seemed to settle down and was more comfortable the next morning. About 12 noon she vomited again, this time a large quantity of upper small-intestine content. A diagnosis of acute intestinal obstruction by gall-stone was made.

Operation was performed under gas, oxygen, and ether anæsthesia. The abdomen was opened through a trans-rectus incision on the right side, above and below the umbilicus. Some free fluid was found in the peritoneal cavity. There were distended loops of bowel above in the jejunum, and collapsed loops in the ileum. The collapsed loops were traced

backwards to what was taken to be the middle of the small intestine, where an impacted gall-stone was found firmly gripped by the bowel. It was about the size of a pigeon's egg. An attempt was made to push it down into the healthy part of the small intestine, but this was not successful, and the stone was pushed upwards into the distended bowel. The collection of fluid in the upper small intestine was seen rushing into the collapsed intestine below; this process was allowed to go on for two or three minutes, and it very materially emptied the distended loops of bowel. Clamps were applied above and below the stone, the bowel incised longitudinally, and the stone removed. The bowel was closed in two layers longitudinally. The gall-bladder region was palpated along with the common bile-duct and the duodenum, and beyond a marked thickening in the region of the common bile-duct nothing grossly abnormal could be made out. The gall-bladder certainly was quite normal in size and shape, and was not adherent. The abdominal wall was closed in layers, and the patient returned to bed.

Rectal salines were given for the first twenty-four hours, and then a purge of calomel with magnesium sulphate. The bowels acted freely and the patient made an uninterrupted recovery and left hospital twelve days after the operation.

Case 9.—Mrs. Clara B., aged 73, a widow, had spent most of her life in Australia, and came over to England in 1929, at the age of 72, to see her only surviving son, who lived in Surrey. She had always led an active life and was insistent that her trouble began while she was on the boat during the voyage to England. During the voyage she became consti-pated, suffered from dyspepsia, and went completely off her food, but she did not vomit at all. She lost over a stone and a half in weight during the voyage, and on arrival in England weighed 11 stone 8 lb. She was seen by several doctors, who put her on various diets and, medicines, but without much benefit. She came up to London in January, 1930, with the express purpose of being X-rayed. However, on the way up from Surrey in a car, she was seized with acute abdominal pain and fainted. She was taken to a nursing home and put to bed. Vomiting was incessant, and the abdomen became distended. Rectal examina-tion did not reveal any abnormality in the rectum or pelvic cavity. The stomach was washed out, and operation was performed the same night under spinal anæsthesia. A right paramedian incision was made, and on opening the abdominal cavity, some blood-stained fluid escaped. Loops of dilated small intestine were seen; the cæcum was collapsed. A finger was passed down into the pelvic cavity and a hard mass was felt in a loop of small gut. The loop was brought outside the abdomen, and the gall-stone removed by making a longitudinal incision along the antimesenteric border of the gut. The wound in the bowel was closed by a double row of sutures; the loop was found to be the lower ileum, about 5 ft. from the ileocæcal valve. The abdominal wound was closed in layers.

Recovery was uneventful, and the patient returned to Surrey fifteen days after the operation. Six months later she was in good health and was contemplating returning to Australia. This patient died in 1932 from pneumonia, some two years after her operation, at the age of 75.

Case 10.—Phyllis K., aged 44, was admitted to hospital on Dec. 12, 1931. On admission she was suddenly attacked with acute abdominal pain which came on in spasms. She gave a history of having been troubled with flatulence, and about three weeks prior to admission had an attack of jaundice which passed off. She had vomited on several occasions, at first green bile and then yellow material. She complained bitterly of thirst. She had nine children.

On examination the patient was grossly fat. The pulse and temperature were normal. The woman was very slightly cyanotic. Very little could be made out from abdominal palpation. An actual diagnosis of acute intestinal obstruction by gall-stone was made in this case.

Operation was performed under gas, oxygen, and ether anæsthesia. The abdomen was opened through a rectus slide-out incision on the right side, above and below the umbilicus. Free fluid was found in the peritoneal cavity. The cæcum was delivered and found empty; the small intestine above it was entirely empty. One could feel distended loops of small intestine above. The small intestine was traced backwards for about 6 to 8 in., when a large gall-stone, about the size of a hen's egg, was found firmly impacted in the bowel. At first

it was difficult to move it at all, but finally it was milked upwards into the distended portion of the bowel, and the bowel was squeezed empty with the fingers. Clamps were applied on each side of the stone, and the bowel incised longitudinally. A large foul stone was removed; it was quite soft and mushy. The hole in the bowel wall was closed longitudinally in this case by the two-layer method. The gall-bladder region was palpated, but one could not satisfactorily make out the gall-bladder itself, as the whole area seemed to be bound up in a mass of adhesions. The abdominal wall was closed in layers.

The patient was given copious rectal salines for three days after the operation and made an uninterrupted recovery. She left hospital sixteen days after the operation.

Case 11.—F. M. H., aged 81 years, a married woman, was seized with colicky abdominal pain in the evening of Nov. 30, 1934. She vomited profusely and her bowels were confined. Her past history was negative, except for an illness four years previously, when she had had abdominal pain and an enlarged liver. She was not jaundiced at that time (*see below*). This illness had been diagnosed as a ' malignant liver ', and a poor prognosis given. Careful questioning in the light of subsequent findings revealed no further history of biliary trouble.

On examination the patient was found to be thin and wasted, and her general condition was poor. The vomiting had ceased temporarily and the bowels were opened after an enema; much flatus was passed. The abdomen was lax and flabby. There was definite tenderness in the left iliac fossa, where a hard lump could be palpated. This was taken to be a string type carcinomatous stricture of the sigmoid colon. Rectal examination revealed tenderness high up on the left side. A diagnosis of acute obstruction due to carcinoma of the colon was made. Salines were administered, and twelve hours after admission, the patient seemed sufficiently improved to stand operation. It was decided to perform a Paul's type of colostomy. The abdomen was opened through a left-sided muscle-splitting incision, when the lump at once presented, and was found to be ileum containing a large gall-stone (*see Fig.* 251). The stone was firmly impacted and could not be dislodged. The bowel was accordingly opened over the stone, which was extracted. The bowel was allowed to empty on the table, and the wound was then closed by the two-layer method.

For two days the patient rallied and it appeared that she would recover. Then her urinary output diminished in spite of salines. She became increasingly uræmic, and was comatose five days after the operation. She developed a fæcal fistula on the sixth day, and died on the eighth day in coma.

Comment.—It seems reasonably certain that the attack of abdominal pain four years previously was one of cholecystitis, and that the ' big liver ' felt and diagnosed as a malignant liver, was actually an enlarged gall-bladder. The gall-bladder then became adherent to the duodenum, and during the last four years a fistula insidiously developed. The post-mortem findings are shown well in *Figs.* 257 and 258, revealing a typical cholecyst-duodenal fistula. The stone removed (*Fig.* 251) could not be returned through the fistula, which had contracted considerably. It weighed 14 grm. when dry.

SUMMARY

1. The frequency of gall-stone obstruction of the intestine is discussed in relation to other cases.

2. Eleven cases of gall-stone obstruction are reported, their clinical features described and analysed.

3. Gall-stones may impact in any part of the intestinal canal and rarely find their way into other viscera.

4. Double obstruction by gall-stones is discussed as a matter of practical importance. The type of stone in such cases is barrel-shaped with a terminal facet. A search should always be made for other stones in cases of intestinal obstruction due to gall-stones.

5. Specimens showing three different types of biliary fistula are described.

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LYMPHATIC SPREAD IN CANCER OF THE RECTUM

By W. B. GABRIEL

SURGEON, ST. MARK'S HOSPITAL, LONDON

CUTHBERT DUKES

PATHOLOGIST, ST. MARK'S HOSPITAL, LONDON

and H. J. R. BUSSEY

RESEARCH ASSISTANT, ST. MARK'S HOSPITAL, LONDON

IN cases of cancer of the rectum treated by radical excision the prognosis depends to a large extent on whether or not the lymphatic glands contain metastases. Our follow-up records at St. Mark's Hospital now show that in the *A Group*[1] of cancer of the rectum, when the growth is removed by perineal excision before there is gross extension to the perirectal tissues, 91 per cent of the operation survivals are alive after five years. In the *B* cases, in which the growth has extended by direct spread to the perirectal tissues but has not caused deposits in the glands, 64 per cent of patients survive for five or more years. On the other hand, in the *C Group*, with glandular metastases, only 16 per cent of patients surviving perineal excision reach the five-year limit. *Table I* shows the results in the three groups set out clearly, the figure in the last column being obtained from the customary fraction—

$$\frac{\text{Alive at 5 years} \times 100}{\text{Operation survivals less those untraced and died from other causes}}$$

Table I.—RESULTS OF PERINEAL EXCISION AT FIVE YEARS CLASSIFIED ACCORDING TO EXTENT OF SPREAD OF THE GROWTH

CLASSIFICATION OF GROWTH	TOTAL No. OF CASES 1927– MAY, 1930	DIED FROM OPERATION	DIED UNDER 5 YEARS		UNTRACED	ALIVE AT 5 YEARS	PERCENTAGE OF 5-YEAR SURVIVALS
			Of Other Causes	Of Cancer			
A	24	–	2	2	–	20	91
B	36	1	5	10	2	18	64
C	34	6	3	21	–	4	16

These figures justify the conclusion that in the *A* cases and in the majority of the *B* cases the surgical treatment has succeeded in eradicating the disease. It is obvious that this does not hold for the cases with glandular spread, for among the *C* cases relatively few patients are alive for three or four years after perineal excision of the rectum.

Since so much depends on whether or not the glands contain metastases we decided to make a gland dissection of every rectum excised for malignant disease. Our plan has been to dissect out and remove each gland separately for

microscopic section, marking the position of each on a scale drawing or photograph. We have applied this method in 100 cases : 70 perineo-abdominal and 30 perineal specimens. These dissections have shown very clearly which are the first glands to receive metastases and in which direction the lymphatic spread normally proceeds (*Table II*).

Table II.—Classification of 100 Gland Dissections

	A	B	C	Total
Perineal excisions	0	9	21	30
Perineo-abdominal excisions ..	7	22	41	70

METHOD OF GLAND DISSECTION

It is possible to make a very complete examination of the extent of spread of cancer of the rectum from operation specimens. The whole rectum and anal canal are removed surrounded by the perirectal tissues and enclosed in the fascia propria or sheath of the rectum. The principal lymph glands lie embedded in the perirectal fat, the connecting lymphatic vessels running beside the main divisions of the superior hæmorrhoidal artery. The perineo-abdominal operation results in the removal of the pelvic colon also, together with a chain of glands at a higher level than is reached by perineal excision.

Fig. 261. — Operation specimen stretched on frame for fixation.

Glandular dissection is much facilitated if the operation specimen is opened up with scissors along the anterior rectal wall and stretched out before fixation. Our method has been to use a rectangular frame composed of meccano perforated strips with an adjustable cross-bar. Attachment to this frame was secured by stitching with needle and twine, the sutures being kept taut so that the specimen retained its normal length and breadth (*Fig. 261*). The ligature round the inferior mesenteric pedicle was also tied to the upper end of the frame in order to keep the vessels taut. Stretched on this frame the specimen was immersed for one to two days in a tall jar containing 10 per cent formalin.

A certain amount of patience is necessary in carrying out the gland dissection. In some of our perineo-abdominal excision specimens we have found as many as 60 glands, and the average has been 28. The exact position and size of each gland was marked on a natural-size drawing, using calipers to ensure accuracy in measurement. As far as possible each gland was bisected and one half taken for section, the other being left *in situ*; but with

some of the smaller glands it was necessary to take all for section. The glands were blocked in batches of five. After microscopic examination the position of metastases was marked on the map by inking in the affected glands.

We have used this method of gland dissection in 100 cases, comprising specimens removed by each of the methods of excision of the rectum mentioned above. The dissection of the 30 perineal specimens has been of value in revealing the distribution of cancerous metastases in the immediate vicinity of the growth and the terminal divisions of the superior hæmorrhoidal vessels, but such specimens did not allow an examination to be made of the glands at a higher level. We have learnt more of the distribution of glandular metastases in the upper hæmorrhoidal, inferior mesenteric, and paracolic glands from the dissection of the 70 perineo-abdominal specimens.

LYMPHATIC DISSEMINATION

Frequency of Lymphatic Metastases.—In the total 100 cases glandular metastases were found in 62, the proportion of the metastases in each group of operation specimens being approximately the same.

We were surprised to find in what a high proportion of these cases only a few glands contained metastases. Thus in the total 62 *C* cases one affected gland was found in 13 cases, 2 glands only in 11 cases, and 3 glands only in 7—that is to say, in half the cases with glandular metastases the cancerous deposits were limited to one, two, or three glands only (*Table III*).

Table III.—Number of Glandular Metastases Observed
in 62 *C* Cases

Cases with one gland only affected ..	.. 13
Cases with two glands only affected ..	.. 11
Cases with three glands only affected	.. 7
Cases with four or more glands affected	.. 31

The fact that so many patients received surgical treatment in the early stages of glandular dissemination is fresh evidence that rectal cancer spreads slowly from gland to gland. If lymphatic spread had been rapid we should have expected to find the cases falling mostly into the groups with no glands or with several glands involved.

From the surgical point of view it is encouraging to reflect that even when lymphatic dissemination has commenced there is usually a considerable period before the growth may be expected to have spread by lymphatic channels beyond the limits of surgical removal.

Course of Lymphatic Dissemination.—We have been much impressed by the orderly and predictable course of lymphatic spread. The first glands to receive metastases are those situated in the perirectal tissues on the same level or immediately above the primary growth. The next to be affected are the chain of glands accompanying the superior hæmorrhoidal vessels. As a rule these are invaded in sequence from below upwards. In an advanced case the metastases come to form an unbroken chain from the regional lymph-nodes to the glands situated at the point of ligature of the inferior mesenteric vessels.

In all but one of the specimens we have dissected the lymphatic spread has

been by such an uninterrupted upward extension. In the single exception carcinomatous metastases were found in one gland near the point of ligation of the blood-vessels although the chain of glands between this point and the growth were free from deposits (*Case* 19). Wood and Wilkie[2] also reported six cases in which the tumours were situated low down in the rectum and the glands near the upper end of the rectum contained metastases, whereas those near the growth were free. Such apparently discontinous lymphatic extension is found in only a small proportion of cases and may be due to an unusual arrangement of the lymphatic vessels.

We have made a special study of the paracolic glands in order to decide whether or not these ever contain metastases in cancer of the rectum. Miles[3] states that the paracolic glands, situated along the mesenteric border of the pelvic colon, are often the seat of metastatic deposits. This has not been our experience; in fact, we have found metastases in the paracolic glands only in one case. This was a very advanced carcinoma in which metastases were present in all the rectal and hæmorrhoidal lymph-nodes, and the ascending lymphatic vessels were all permeated by a continuous growth of cancer cells. In this specimen we found metastases in one of the paracolic glands and also a downward extension of the growth in the perirectal tissues (*Case* 24). We agree with Miles that lymphatic extension to the paracolic glands is due to blockage of the normal lymph-stream by metastatic deposits, but by the time this has occurred it is unlikely that the disease can be eradicated by surgical excision.

The normal course of lymphatic dissemination may be summarized as follows: the first glands to be affected are those in the immediate vicinity of the growth, after which a continuous spread takes place along the glands accompanying the superior hæmorrhoidal vessels. Until these lymphatic channels are all blocked no downward or lateral lymphatic spread is found, but when carcinomatous metastases are present in all the hæmorrhoidal glands then there may be extension in other directions.

Detection of Glandular Metastases.—In the course of these dissections we have examined more than 2000 lymph glands and thus have had exceptional opportunity for observing to what extent it is possible to determine from the gross characters whether or not lymphatic glands contain metastases. We have made this question the object of special investigation in 1242 glands removed from perineo-abdominal specimens. Our plan was to note during the course of dissection whether or not each gland was judged to contain metastases and then compare the estimate with the verdict which was given later by microscopic examination.

Of these 1242 glands, 905 were considered from gross characters to be negative, but subsequent microscopic examination showed 18 to contain metastases—an error of 2 per cent. On the other hand, in the 337 glands which were judged positive from their gross characters metastases were present actually in only 132, a mistake being made in 205 cases, or 61 per cent of the total. Since a surgeon is inclined to be so much influenced by the discovery of enlarged glands it is important that he should know that conjectures with respect to metastases in the rectal, hæmorrhoidal, or paracolic glands are more often wrong than right. The commonest source of error consists in presuming glands to contain metastases which are enlarged as a result of inflammation.

GLANDULAR DISSECTION AS AN AID TO PROGNOSIS

We have already pointed out that although the general prognosis for patients with glandular metastases is poor, our records show that a certain proportion survive for several years. An apparent though not of course complete explanation of this is that the survivors are patients in whom the lymphatic spread was actually limited to the tissue removed at operation, whereas the deaths occurred amongst those in whom the lymphatic spread had reached a higher level. The method of gland dissection we have adopted now allows a distinction to be drawn between these two groups of cases and a more accurate prognosis based on an examination of the operation specimen. Those cases in which the glandular spread has reached up to the level of the point of ligature of the blood-vessels we classify as $C\,2$ cases.
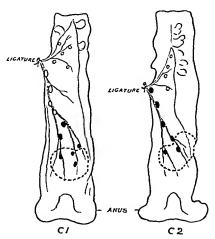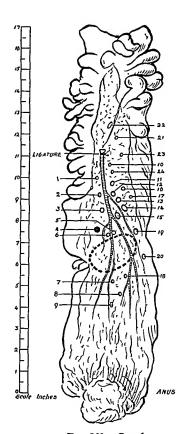
FIG. 262.—Showing examples of $C1$ and $C2$ cases.

In these cases the prognosis is bad, there being reason to suspect that glands at a higher level are affected. On the other hand, cases in which the regional lymph glands only are involved, or those in which the upward spread has not yet reached the glands at the point of ligature of the blood-vessels, we classify as $C\,1$ (*Fig.* 262). The prognosis is much better for this group, since the disease does not yet appear to have spread by lymphatic channels to the limits of the tissue removed. The application of this method of classification to the 62 cases is recorded in *Table IV*.

Table IV.—SUBDIVISION OF C CASES

	$C\,1$	$C\,2$	TOTAL
Perineal excision ..	13	8	21
Perineo-abdominal ..	30	11	41

This system of classification takes account only of metastases in lymphatic glands. In a few cases we have found deposits of carcinoma cells at a distance

FIG 263.—*Case 1.*

Case 1.—H. B. E., male, aged 67. A deeply ulcerated growth 2 in. in diameter in the upper third of the rectum. Adenocarcinoma grade 3: metastases in one regional gland. *C* 1 case. (*Fig.* 263.)

Case 2.—W. S., male, aged 67. An ulcerating colloid carcinoma 3 in. in diameter extending completely round the upper third of the rectum. Another small deeply ulcerated adenocarcinoma 1 in. in diameter was present on the right lateral wall just above the main tumour. Spread by direct continuity into the perirectal tissues. Metastases of colloid carcinoma present in one gland. *C* 1 case. (*Fig.* 264.)
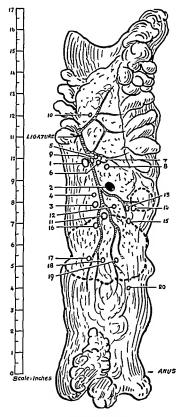
FIG. 264 —*Case 2.*

Case 3.—Mrs. L. D., aged 59. A deeply ulcerated growth 2½ in. in diameter in the recto-sigmoid region, with gross evidence of extra-rectal spread. Adenocarcinoma grade 2. Metastases present in one gland. *C* 1 case. (*Fig.* 265.)

FIG. 265.—*Case* 3.
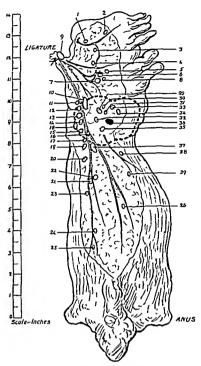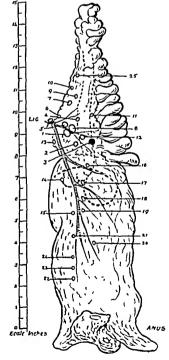
Case 4.—Mrs. N. D., aged 57. A huge fungating growth in the recto-sigmoid region. Adenocarcinoma grade 2. Metastases present in one gland only. *C* 1 case. (*Fig.* 266.)

FIG 266 —*Case* 4.
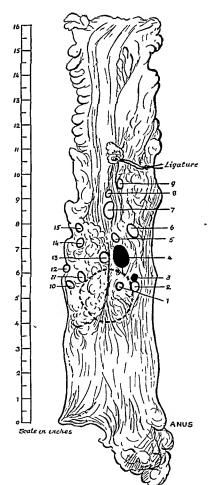
FIG. 267.—*Case* 5.

Case 5.—Mrs. E. C., aged 30. An ulcerating growth 2 in. in diameter in the upper third of the rectum. Adenocarcinoma grade 2. Metastases present in two glands. *C* I case. (*Fig.*267.)

Case 6.—Mrs. E. F., aged 42. An oval ulcerating growth 3 in. in the long axis extended two-thirds round the ampulla of the rectum. Adenocarcinoma grade 2. Metastases present in two lymph-nodes situated immediately above the growth. *C* I case. (*Fig.* 268.)
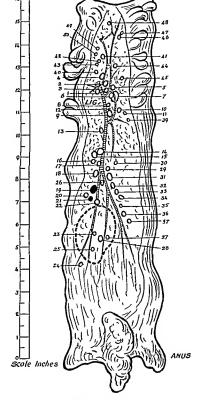
FIG. 268 —*Case* 6.

Case 7.—F. B., male, aged 63. An oval ulcerating growth 3 in. in transverse diameter situated in the middle third of the rectum. Adenocarcinoma grade 2. Metastases present in three regional lymphatic glands. *C* I case. (*Fig. 269.*)
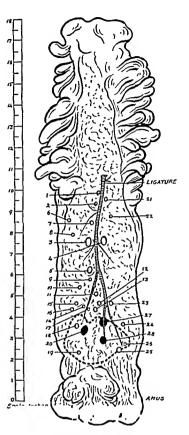
FIG. 269.—*Case 7.*
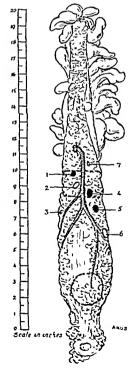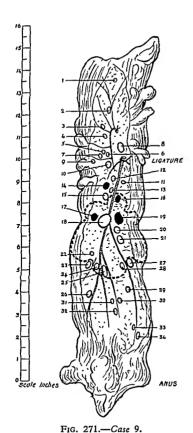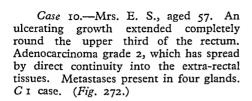
FIG. 270.—*Case 8.*

Case 8.—S. B., male, aged 66. Two ulcerating growths were present, one in the lower third, the other at the recto-sigmoid junction. Both adenocarcinoma. The upper grade 2, the lower grade 3. Metastases present in three glands. *C* I case. (*Fig. 270.*)

FIG. 271.—*Case 9.*

Case 9.—Miss M. S., aged 34. An ulcerating growth 3½ in. in long axis extended completely round the upper third of the rectum with gross evidence of extra-rectal spread. Adenocarcinoma grade 2. Metastases present in three of the regional glands and in one gland immediately above the growth. *C* I case. (*Fig.* 271.)

Case 10.—Mrs. E. S., aged 57. An ulcerating growth extended completely round the upper third of the rectum. Adenocarcinoma grade 2, which has spread by direct continuity into the extra-rectal tissues. Metastases present in four glands. *C* I case. (*Fig.* 272.)
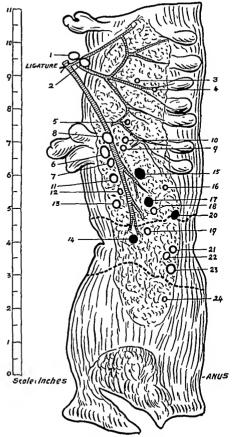
FIG. 272.—*Case 10.*

Case 11.—R. T., male, aged 63. An oval ulcerating growth 3 in. in diameter in the upper third of the rectum. Adenocarcinoma grade 2, with metastases in six regional glands. This patient died of paralytic ileus on the fourth day and at the post-mortem a small secondary deposit was found in the centre of the liver, presumably due to venous spread. *C* I case. (*Fig.* 273.)
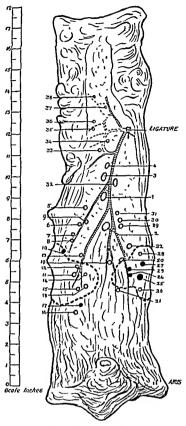
FIG. 273.—*Case* 11.
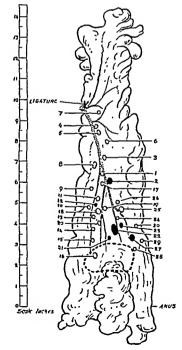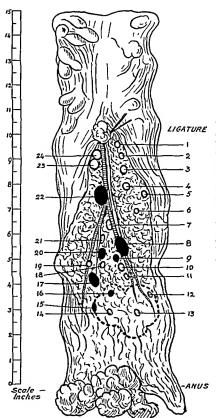
FIG. 274.—*Case* 12.

Case 12.—Mrs. S. R., aged 61. An oval ulcerating growth 2 in. in its long axis extended half round the middle of the rectum, with gross evidence of extra-rectal spread. Adenocarcinoma grade 3. Metastases present in six glands. *C* I case. (*Fig.* 274.)

FIG. 275.—*Case* 13.

Case 13.—T. G., male, aged 47. A deeply ulcerated growth about 2½ in. in diameter was present in the lower third of the rectum, with gross evidence of extra-rectal spread. Adenocarcinoma grade 2. Although metastases were present in seven out of twenty-four glands examined, with a large infected gland at the point of bifurcation of the superior hæmorrhoidal vessels, this case can be grouped *C* I because there still remain five uninfected hæmorrhoidal glands in the 2 in. which intervene between the upper infected gland and the point of ligation of the inferior mesenteric pedicle. (*Fig.* 275.)

Case 14.—Mrs. E. D., aged 61. An ulcerating growth 3 in. in diameter in the middle third of the rectum. Adenocarcinoma grade 2. A chain of ten glands containing metastases was present along the superior hæmorrhoidal vessels to within 2 in. of the main ligature. *C* I case. (*Fig.* 276.)
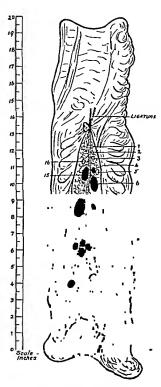
FIG. 276 —*Case* 14.

Case 15.—Mrs. A. W., aged 55. An oval ulcerating growth present in the middle of the rectum. Adenocarcinoma grade 2 with colloid degeneration. Extra-rectal tissues penetrated by direct spread and metastases present in eleven glands. *C* 1 case. (*Fig.* 277.)

FIG. 277.—*Case* 15.
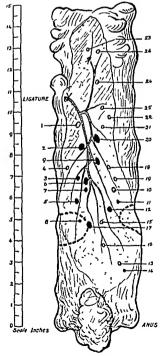
FIG. 278 —*Case* 16.

Case 16.—Mrs. M. A., aged 68. A projecting semi-ulcerated growth 1½ in. in diameter in the upper third of the rectum, with macroscopic evidence of extra-rectal spread. Adenocarcinoma grade 3. Metastases present in eleven regional and superior hæmorrhoidal glands. *C* 1 case. (*Fig.* 278).
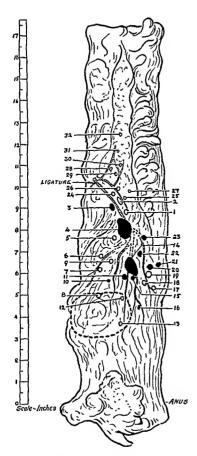
FIG. 279.—*Case* 17.

Case 17.—J. K., male, aged 73. A flat, oval, projecting growth, 3 in. in its transverse axis, extended three-quarters round the middle of the rectum, being situated on the posterior, left lateral, and anterior quadrants. Gross evidence of extra-rectal spread. The tumour is a colloid carcinoma. Metastases present in eleven glands. *C* I case. (*Fig.* 279.)

Case 18.—Mrs. A. R., aged 40. An ulcerating growth 2½ in. in diameter extended completely round the lower third of the rectum, with gross evidence of extra-rectal spread. Adenocarcinoma grade 3. Metastases present in sixteen lymph glands. *C* I case. (*Fig.* 280.)
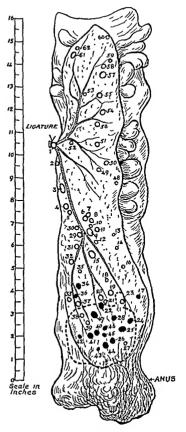
FIG. 280.—*Case* 18.

Case 19.—Mrs. Elizabeth H., aged 70. A flat, semi-ulcerated growth 1½ in. in diameter in the lower third of the rectum. Section proves this to be a colloid carcinoma which has spread to the extra-rectal tissues. Metastases present in one gland near the ligation of the inferior mesenteric pedicle. Seven glands below this are free from metastases. *C* 2 case. (*Fig.* 281.)
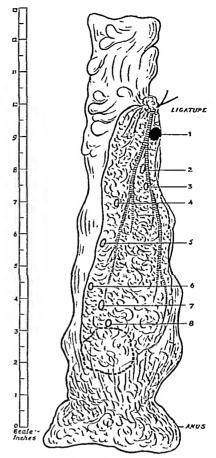
FIG. 281.—*Case* 19.
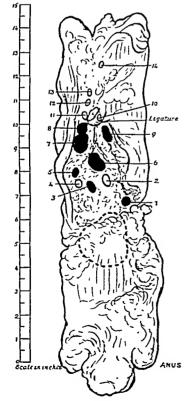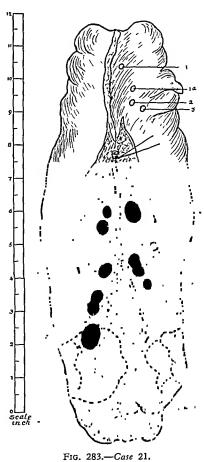
FIG. 282 —*Case* 20.

Case 20.—C. G., male, aged 50. A fungating growth 2½ in. in diameter in the middle third of the rectum. Adenocarcinoma grade 2 which has spread by direct continuity to the extra-rectal tissues. Metastases present in seven regional and superior hæmorrhoidal glands. Four para-colic glands free from metastases. *C* 2 case. (*Fig.* 282.)

FIG. 283.—*Case* 21.

Case 21.—H. G., male, aged 53. An ulcerating growth 2 in. in diameter extended round the lower third of the rectum. Adenocarcinoma grade 2. Metastases present in eight regional and superior hæmorrhoidal glands. Four paracolic glands free from metastases. *C* 2 case. (*Fig.* 283.)

Case 22.—Mrs. Elsie H., aged 42. A flat ulcerating growth $2\frac{1}{2}$ in. in diameter extended almost completely round the middle of the rectum. Adenocarcinoma grade 3. Metastases in eleven glands. *C* 2 case. (*Fig.* 284.)
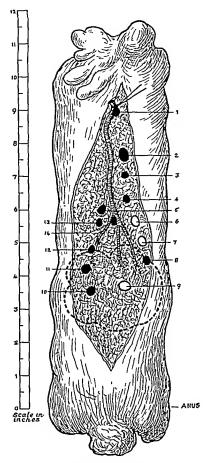
FIG. 284.—*Case* 22.

Case 23.—Miss P. L., aged 71. A huge ulcerating growth 3 in. in diameter extended completely round the recto-sigmoid junction. Adenocarcinoma grade 3. Eighteen regional and superior hæmorrhoidal glands contain metastases, including the glands situated at the point of ligation of the inferior mesenteric pedicle. Malignant invasion of superior hæmorrhoidal vein also proved to be present. Three paracolic glands free from metastases. *C* 2 case. (*Fig.* 285.)

Fig. 285.—*Case* 23.

Fig 286.—*Case* 24.
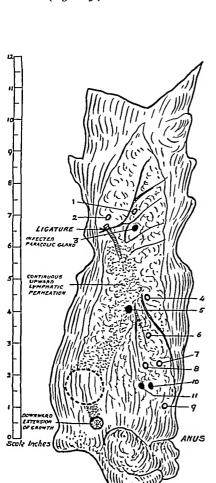
Case 24.—J. W., male, aged 40. A deeply ulcerated growth less than 1 in. in diameter was situated in the lower third of the rectum, with macroscopic evidence of massive extra-rectal spread. Adenocarcinoma grade 3. Section revealed a continuous mass of upward spread involving glands, lymphatic trunks, and veins. One paracolic gland contained growth. *C* 2 case. (*Fig.* 286.)

from the primary growth although the lymphatic glands themselves have been free. Most of these non-lymphatic metastases are the result of vascular spread. Whenever the lymphatic glands have been free we have grouped the operation specimens as *B* cases and excluded them from consideration in this paper.

ILLUSTRATIVE CASES AND SURGICAL APPLICATION

The characters and course of lymphatic spread can be shown by a series of cases illustrating various degrees of glandular involvement. For this purpose we have selected 24 cases all from the practice of one surgeon (W. B. G.) who carried out the operation in 38 of the perineo-abdominal excisions by the one-stage method previously described (Gabriel[4]). In each case a drawing was prepared by Mr. S. A. Sewell, with strict attention to scale to show the following details : (1) The total length of the specimen from the anus to the iliac colon ; (2) The level of ligation of the inferior mesenteric pedicle ; (3) The situation and size of the primary growth, indicated by dotted lines ; (4) The level of bifurcation of the superior hæmorrhoidal artery ; (5) The exact position, shape, and size of each lymph-node dissected out, those proved to contain metastases being marked in black. These 24 cases have been arranged according to the degree of the glandular involvement, beginning with solitary regional metastases and ending with involvement of all the hæmorrhoidal lymph glands. (*Figs.* 263-286.)

Among these 24 cases 18 proved to be *C* 1 and 6 *C* 2. This high proportion of *C* 1 cases is of practical importance and gives the surgeon much encouragement in performing a combined excision of the rectum, even in cases so far advanced as to be of borderline operability. For instance in *Case* 2 the growth was so large and mobility so restricted that little hope was entertained of its being operable, but radical excision by the one-stage perineo-abdominal method proved possible and successful, and by our routine examination metastases have been proved to be present in only one gland at a distance of 9 in. from the anus.

In regard to the extent of lymphatic spread and the radical extirpation of rectal cancer our investigations show the overwhelming importance of the main path of upward lymphatic spread along the superior hæmorrhoidal vessels. In the cases of perineo-abdominal excision illustrated in this article the inferior mesenteric pedicle was ligated at an average height of 10 in. from the anus. When metastases are present in the hæmorrhoidal lymph glands it is obviously advantageous to ligate the vascular and lymphatic pedicle at as high a level as possible.

SUMMARY

1. A method is described for the examination of operation specimens of cancer of the rectum in order to determine the extent of lymphatic spread.

2. As a rule the regional lymph glands are the first to be affected by metastases in cancer of the rectum. Lymphatic spread then proceeds from below upwards along the chain of glands accompanying the superior hæmorrhoidal artery. Irregular or interrupted spread is very uncommon. Lateral or downward lymphatic spread is only found in a late stage of the disease when the hæmorrhoidal lymphatics are blocked by metastases.

3. Examination of operation specimens in the manner described permits a distinction to be made between cases in which glandular spread has already reached the glands at the point of ligation of the inferior mesenteric pedicle (C 2 cases) and those in which the upward spread has not extended to this point (C 1 cases). We expect that our follow-up records will show that the prognosis in C 1 cases is much better than in C 2.

4. In the 100 gland dissections we found lymphatic metastases in 62 cases. This is a slightly higher proportion than is usually reported in any series of operation specimens of cancer of the rectum, but it is encouraging to record that the dissection of 70 specimens removed by perineo-abdominal excision showed that only a small proportion (11 out of 70) belonged to the C 2 *Group* in which the disease had actually spread by lymphatic channels to the limit of surgical removal.

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THE RÔLE OF SYMPATHECTOMY IN THE TREATMENT OF PERIPHERAL VASCULAR DISEASE*

BY R. I. HARRIS

ASSOCIATE SURGEON, TORONTO GENERAL HOSPITAL, TORONTO

OF all the functions of the sympathetic nervous system, that which controls the flow of blood through peripheral arterioles, if not the most important, is at any rate the most conspicuous and the easiest to study. For this reason the present revival of interest in surgery of the sympathetic nervous system has centred largely around the changes in blood-flow which may be caused by appropriate operations on sympathetic nerves. The increasing incidence, or at any rate the increasing recognition, of cases of peripheral vascular disease at a time when interest in the effect of operations upon sympathetic nerves was aroused has led naturally to the use of sympathectomy in the treatment of such diseases. This paper reports our experiences in the treatment of certain peripheral vascular diseases (especially Buerger's disease) by means of sympathectomy.

In all of the three common peripheral vascular diseases (Raynaud's disease, Buerger's disease, and peripheral arteriosclerosis) vasospasm is an element of greater or less importance. In Raynaud's disease the essential basis of the diminished blood-flow is vasospasm. In Buerger's disease and peripheral arteriosclerosis, while the essential lesion is mechanical occlusion of the lumina of certain vessels, there may be a superimposed element of vasospasm. This is of the greatest clinical importance since upon it is based the only form of surgical treatment which offers any hope of success—namely, sympathectomy.

Sympathectomy produces improvement in the obliterative vascular diseases by dilating to their maximum such vessels in the involved extremity as are in spasm. We have no evidence that it causes any change in the occluded vessels. The operation is of value only in those cases in which the accompanying vasospasm is of considerable degree. It becomes important therefore to be able to determine before operation the degree of vasospasm present. This can best be done for the lower extremity by temporary paralysis of the sympathetic nervous system by means of a spinal anæsthetic. The increase in blood-flow which results from this procedure can be measured by the rise in skin temperature of the feet (*Fig.* 287). For the upper extremity, novocain block of a peripheral nerve (e.g., the ulnar) will cause sympathetic paralysis in the sensory area of the nerve, and its effect can similarly be measured by the changes in skin temperature it produces.

On the basis of a personal experience which now extends over about seventy-five cases, it can be definitely stated that these pre-operative tests give information which indicate with considerable accuracy the benefit which may be expected

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from sympathectomy. Generally speaking, the result of operation is somewhat more favourable than might be expected from the preliminary investigation. All patients whose pre-operative tests resulted in an appreciable rise in skin temperature obtained definite benefit from sympathectomy. Frequently the improvement was dramatic. Certain patients in whom the preliminary test produced slight rise in skin temperature obtained an appreciable increase in circulation—sufficient to turn the scale from impending gangrene to rapid healing and to restore the ability to undertake limited activity.
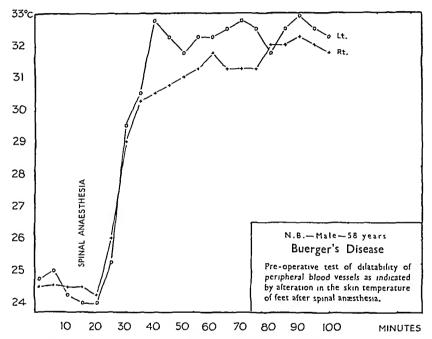
FIG. 287.—A graph of the changes in the skin temperature of the feet following the induction of spinal anæsthesia, indicating a high degree of associated vasospasm and a suitable case for the operation of lumbar sympathectomy.

BUERGER'S DISEASE

In the past four years twenty-four cases of Buerger's disease have been treated by sympathectomy in the Toronto General Hospital. The operations have all been lumbar sympathectomies for the treatment of the disease in the lower extremities, with the exception of three cases in which stellate ganglionectomy was performed for the treatment of the disease in the upper extremity. The ages ranged from 22 to 60 years, the average age being 36 years. All were males. The result of treatment of their disease by sympathectomy has been recently investigated, and the outcome of this investigation is given below. In attempting to judge the benefit obtained by operation we have classified the results in four groups as follows :—

1. *Result good and maintained to the present time.* The immediate result of operation was an appreciable increase in circulation of the extremity as evidenced

by increased temperature, improvement in colour, relief of pain, disappearance of trophic changes, and the healing of ulcers and gangrenous patches. Function was improved so that the patient could return to work or at least could undertake much greater activity than previously. Intermittent claudication, if present, disappeared. This beneficial result is still maintained.

2. *Immediate result good, but too short a time has elapsed to permit accurate assessment of the permanent result.* In all probability the majority of this group will eventually be placed in Group 1.

3. *Immediate result good, but late recurrence has taken place.* The progress of the disease, after varying intervals of time, has caused recurrence of symptoms, disability, and often amputation.

4. *Result poor.* Sympathectomy did not result in any improvement in symptoms, or the persistence of one serious symptom, such as rest-pain, necessitated amputation.

Classified in this manner the results are shown in tabular form in *Table I.*

Table I.—SUMMARY OF THE RESULTS OBTAINED BY SYMPATHECTOMY IN 24 CASES OF BUERGER'S DISEASE

	GOOD	IMMEDIATE RESULT GOOD. TOO RECENT TO JUDGE END-RESULT	IMMEDIATE RESULT GOOD. LATER RELAPSED AND LIMB AMPUTATED	POOR
Number of cases ..	14	5	2	3
Percentage of total ..	58·3	20·8	8·4	12·2
Average age ..	41	37	28·5	36
Average rise of skin temperature on pre-operative test ..	6·6° C	5° C.	1° C.	0° C.
Extremes : { Low ..	4° C.	3° C.		
Extremes : { High ..	10° C.	6° C.		

Comment.—Analysis of these results permits important conclusions to be drawn. The most significant evidence is that a considerable number of patients with Buerger's disease can be greatly benefited by sympathectomy. If we include the patients in Group 2 as good results, the number greatly benefited by operation is 79 per cent of the total. The patients in Groups 3 and 4, in which the result was poor, account for 21 per cent of the total. Even here the patients in Group 3 obtained temporary benefit, lasting sometimes two years. They have expressed the opinion that this benefit, though temporary, made operation worth while, even though amputation was later necessary.

The benefit obtained by operation is often dramatic. Not infrequently a patient who is completely crippled by pain and intermittent claudication is so greatly improved that he can return to heavy manual labour. The following is such an illustrative case.

J. J., a Canadian male, 41 years old, was first seen in April, 1932, complaining of pain in the feet and calves. This began five years previously with aching pain in and abnormal coldness of the right foot. The left foot was similarly involved later, and when he was first seen this was the more painful extremity. Severe intermittent claudication occurred after walking two blocks. He had many attacks of migrating thrombophlebitis. Rest-pain was

present in the left foot on admission. He was nearly completely incapacitated by pain and had lost more than 50 per cent of time from his work as a mechanic in the year prior to admission.

Examination on admission showed cold feet with marked postural colour changes. Some lesions of migrating thrombophlebitis were present. There was no pulsation in the pedal arteries of either foot. Spinal anæsthesia caused a rise in skin temperature of 4° C. in the left foot, 6·5° C. in the right foot, indicating an accompanying vasospasm of considerable degree.

As the left leg and foot were the source of much the more severe symptoms, a left lumbar sympathectomy was performed on May 7, 1932. This was followed at once by increased warmth and improved colour of the left foot and the complete disappearance of rest-pain. He returned to work in a few months and continued at this until July, 1933, when he returned of his own accord to have the right side operated upon. During the interval he had worked particularly long hours as mate on a lake freighter, his duties at certain times necessitating his remaining on the bridge for twenty hours at a stretch. A right lumbar sympathectomy was performed on July 12, 1933. Since then he has been continuously at work.

Table I clearly indicates that the result of sympathectomy can be predicted with accuracy from the pre-operative examination. All the patients in Groups 1 and 2 had a rise of skin temperature after the administration of spinal anæsthesia of considerable amount. All the poor results in Groups 3 and 4 had a poor response to spinal anæsthesia. The pre-operative test with spinal anæsthesia provides us with a very accurate measure of the benefit which will be obtainable from sympathectomy.

It is, as yet, too early to predict the ultimate course of these cases. Even though they have been greatly benefited by operation, the basic cause of the occlusive vascular disease remains. It is quite possible that the vascular disease will continue to progress and lead ultimately to recurrence of the disabling symptoms. To date, however, in those cases who have been greatly benefited there has been a gratifying absence of any evidence of progression of the disease. Four years have now elapsed since the earliest case was operated upon. He is still actively engaged in work without evidences of progress of the vascular disease.

PERIPHERAL ARTERIOSCLEROSIS

Though arteriosclerosis usually manifests itself by cerebral, cardiac, or renal lesions, occasionally the most conspicuous lesion is in the extremities. In this event the clinical picture is similar to that of Buerger's disease. An elderly individual of either sex, usually with definite evidence of arteriosclerosis (thickened arteries and increased blood-pressure) begins to display symptoms of diminished blood-supply to the lower extremities. As in Buerger's disease, the vascular lesion here is also occlusive. The degeneration in the media with secondary intimal arteriosclerosis favours thrombosis. Often the onset of symptoms is sudden, as the result of thrombosis in previously damaged vessels. The symptoms are similar to those of Buerger's disease and for similar reasons—muscular fatigue, cold feet, intermittent claudication, postural colour changes, absence of pulsation in the pedal arteries; later rest-pain, trophic changes, and gangrene. In peripheral arteriosclerosis the onset of incapacitating symptoms is apt to be more sudden and more severe than in Buerger's disease because the final factor frequently is thrombosis in a comparatively large vessel. Gangrene, when it occurs, is more massive than in Buerger's disease.

As in Buerger's disease, a certain proportion of the cases of peripheral arterio-sclerosis have an accompanying element of vasospasm, and a proportion of these is capable of sufficient improvement by sympathectomy to justify the operation. The number of suitable cases is not great.   To begin with, arteriosclerosis affect-ing chiefly the extremities is relatively uncommon.   Of this subgroup only a fraction present the accompanying vasospasm which renders them capable of improvement by sympathectomy.   Many cases abruptly develop massive thrombosis with gangrene, which of itself necessitates amputation.   Finally, the suitable lesion by the very nature of its pathology is apt to occur in a patient who is a poor subject for surgery.   He or she is advanced in years.   The active period of his life is probably over, the necessity of work in most cases does not exist.   His peripheral vascular disease is but part of a generalized vascular disease which may at any time present much more serious lesions in brain, heart, or kidney.

In spite of all these limitations one does occasionally see patients who are incapacitated by reason of impaired circulation to the extremities due to arterio-sclerosis, an impairment of circulation which falls short of gangrene, but incapacitates the patient because of pain and intermittent claudication.   Properly selected cases from this group can be benefited by sympathectomy.   Suitability is dependent upon the degree of vasospasm, and this is determined by pre-operative spinal anæsthesia or posterior tibial nerve block.

Results of Sympathectomy.—Twelve cases of peripheral arteriosclerosis have been treated by sympathectomy at the Toronto General Hospital in the past four years.   The result of this treatment is summarized in *Table II*.   For purposes of analysis, the results have been divided into three groups, as follows :—

1. Result good and maintained until the present time.

2. Immediate result good, but further progression of the arterial disease resulted in the return of serious vascular deficiency, usually with gangrene which necessitated amputation.

3. Result poor.   Operation did not cause any appreciable improvement in circulation.

Table II.—Summary of Results Obtained by Sympathectomy in 12 Cases of Peripheral Arteriosclerosis

	Good	Immediate Result Good but Relapse Occurred and Limb Amputated	Poor
Number of cases	5	1	6
Percentage of total ..	41·66	8·4	50
Average age	62	70	64
Average rise of skin tem-perature on pre-operative test	6·2° C.	1·5° C.	0·7° C.
Extremes : { Low ..	3° C.		0° C.
{ High ..	10° C.		3° C.

Comment.—These twelve cases comprise all the cases of peripheral arterio-sclerosis treated by sympathectomy during the period we have been interested in this form of treatement.   The figure includes patients operated upon before

the value of pre-operative tests was established and patients operated upon in spite of unfavourable pre-operative tests in the hope that some benefit might be obtained sufficient to avoid the necessity of amputation. That this hope was not without some justification is evidenced by the single patient in the second group, whose history in summary form is as follows :—

H. L., a Jewish male, 70 years old, for two years prior to admission had been increasingly disabled by cold painful feet, intermittent claudication, rest-pain, and finally gangrene of the tip of the great toe with infection. Colour changes were marked. Posterior tibial nerve block yielded a skin temperature rise of only 1·5° C. Nevertheless, sympathectomy was performed on Nov. 28, 1930, with great benefit. Rest-pain disappeared at once. The gangrenous spot promptly separated and healed. Skin temperature improved. He was able to walk several blocks without discomfort, whereas before operation he was incapacitated by intermittent claudication after walking half a block. This improvement was maintained for a year. Then pain and claudication recurred, though to a less severe degree than before his operation. Two years after operation gangrene again threatened the foot, and for this and for pain his leg was amputated.

Sympathectomy postponed amputation for two years and gave this man one year of complete comfort and another year of comparative freedom from symptoms.

Perhaps the most important finding in this analysis is the evidence that by pre-operative tests it is possible to determine with considerable accuracy the effect of sympathectomy upon a given patient. In every case in which the result of operation was good (Group 1) the pre-operative test resulted in a sharp rise in skin temperature, never less than 3° C., and usually higher, the average rise being 6·2° C. The reverse was true in those cases in which the result of operation was poor (Groups 2 and 3). In all these the pre-operative tests gave feeble increase in skin temperature, never more than 3° C., and usually less. Our experience leads us to feel strongly that in any case of peripheral arteriosclerosis which seems suitable for sympathectomy, pre-operative skin temperature tests, by spinal anæsthesia or posterior tibial nerve block, will determine accurately the benefit which will follow operation.

In the favourable group the benefit obtained is often great, sometimes dramatic. The instant relief from the intolerable rest-pain is very striking and transforms the patient from a sleepless pain-wracked invalid to a contented being. Unhealed wounds and small patches of gangrene rapidly heal. The degree of benefit can best be visualized by the relation of one or two case histories.

J. T., an Englishman, 63 years of age, for a year had been incapacitated by cold painful feet, intermittent claudication, rest-pain, and finally by the onset of gangrene of his right great toe. Postural colour changes were marked. No pulse could be felt in the dorsalis pedis or posterior tibial arteries of either foot. Pre-operative tests gave a rise in skin temperature of 4° C. He refused operation and left hospital. A month later he returned, driven by the intolerable rest-pain to a willingness to submit to anything. The gangrene of the great toe had extended to the metatarso-phalangeal joint. Right lumbar sympathectomy was performed in April, 1930, and the gangrenous toe was disarticulated at the metatarso-phalangeal joint. Operation was followed immediately by complete disappearance of the rest-pain. The wound of the toe slowly healed. It is now three and a half years since operation. The temperature of his right foot is maintained at higher level than the left. He is free from discomfort and leads a life of moderate activity. To date there is no evidence of recurrence of vascular insufficiency.

A. S., a Canadian male, 68 years of age, was incapacitated by intermittent claudication of two months' duration in the left leg. The onset of this had been abrupt, and the symptoms

so severe as to prevent him completely from working as a labourer. There was no pulsation to be felt in the dorsalis pedis artery on either side, but that in the posterior tibial could be felt on both sides. No postural colour changes and no trophic changes or gangrene were observed. Pre-operative test with spinal anæsthesia gave a skin temperature rise of 10° C. Left lumbar sympathectomy was performed in May, 1931, with immediate and very beneficial results. His incapacitating intermittent claudication completely disappeared and he was able to return to work as a labourer. To date, two and a half years after operation, the improvement is maintained. He is still at work and has no symptoms. The warmth of the foot is maintained.

The abrupt onset and the severity of this man's symptoms suggest that the final interference with circulation was thrombosis in a vessel supplying a relatively small field, perhaps chiefly to muscles.

RAYNAUD'S DISEASE

Our experience with the treatment of Raynaud's disease by sympathectomy has been too meagre to permit us to draw any definite conclusions based upon our own patients. Raynaud's disease is uncommon. Though cases of minor severity are occasionally seen, the more severe forms, of a degree which would justify the risk of operation, are very infrequent. Moreover, they may present themselves in bizarre forms which renders classification difficult. This purely vasospastic form of vascular disease should be particularly suitable for treatment by sympathectomy, and the reports in the literature support this contention. Our experience is limited to four cases. One of these conformed exactly to Raynaud's original description—a middle-aged female disabled by recurring attacks of blanching of the fingers induced by cold, followed by painful cyanosis, and resulting in trophic ulcerations of the finger-tips. The remaining three cases presented features in addition to the recurring attacks of vasospasm which complicated the diagnosis. All were benefited by sympathectomy. While our experience with Raynaud's disease is limited, we feel it is singularly suited to treatment by sympathectomy. Case histories of three patients follow :—

J. F., a Canadian male, aged 58 years, had been incapacitated for four years by recurring attacks of painful blanching of the hands and feet followed by purplish discoloration. A trophic ulcer was present on the left leg. An unusual feature was the extreme degree of œdema present in both feet. Pulsation was present in both radial arteries, both dorsalis pedis arteries, the right posterior tibial artery, but was absent from the left posterior tibial artery. Left lumbar sympathectomy was performed with benefit. The ulcer healed promptly and he was made more comfortable. The œdema is unchanged and the attacks of blanching still occur in the hands.

E. S., a Canadian female, aged 24 years, since childhood had suffered from severe attacks of vascular spasm induced by cold and involving all four extremities and all the exposed parts of the body—nose, ears, cheeks, chin, and knees. Trophic changes were very marked. By repeated ulceration she had lost innumerable small patches of skin from the involved parts of the body. Pulsation was present in all the palpable arteries. Pre-operative test by spinal anæsthesia gave a skin temperature rise of 8° C. Right lumbar sympathectomy performed in April, 1931, resulted in well-marked increase in circulation of the right leg and foot, but did not prevent the recurrence of trophic ulceration during the ensuing winter. Improved but not cured by operation.

J. B., an Englishwoman, 57 years of age, for five months prior to admission had suffered from attacks of cyanosis and coldness of the toes of the right foot, especially the little toe. There was no pain or intermittent claudication. Pulsation was felt in all the pedal arteries. Pre-operative test with spinal anæsthesia gave a skin temperature rise of 5° C. Right

lumbar sympathectomy performed in October, 1931, was followed by striking improvement in the involved foot. This case gave promise of a complete cure. The patient, however, developed cerebral thrombosis and died one month after operation.

OPERATIVE TECHNIQUE

It may not be inappropriate here to outline briefly our operative technique, since technical difficulties can be greatly reduced by a proper approach.

Lumbar Sympathectomy.—In removing the lumbar sympathetic chain our preference is for the extraperitoneal approach first advocated by Royle. The transperitoneal approach is not without danger of intraperitoneal complications, and it fails to give adequate exposure of the upper portion of the lumbar trunk.
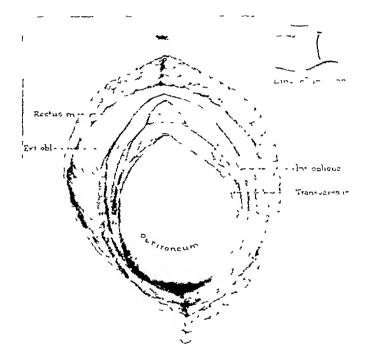
FIG. 288 —The transverse abdominal incision for the extraperitoneal approach to the lumbar sympathetic chain

Royle's oblique incision in the loin necessitates the removal of the chain through a deep narrow wound. In stout adults this can be a difficult technical procedure. For this reason we have modified the approach (*Fig.* 288). Exposure is much superior and the operation much easier if carried out through a transverse incision extending from the umbilicus to the edge of the quadratus lumborum muscle. The three muscles of the anterior abdominal wall are cut through transversely in the line of the skin incision, and the sheath of the rectus is cut without severing the muscle. This permits the peritoneum to bulge into the wound. Hæmostasis is secured and skin towels are applied. With the hand, the peritoneum is swept free

from the lateral and posterior abdominal wall and displaced towards the mid-line. It is a mistake to attempt to free the peritoneum completely from the anterior abdominal wall. It is densely adherent to the posterior sheath of the rectus and to the linea semilunaris. The attempt to separate it here always results in tearing it. The opening in the abdominal muscles is widely retracted upwards and downwards, and the peritoneum with the abdominal viscera held to the mid-line by the assistant's hands. This brings clearly into view the quadratus lumborum and psoas muscles. The ureter is displaced with the peritoneum (*Fig.* 289, 290)
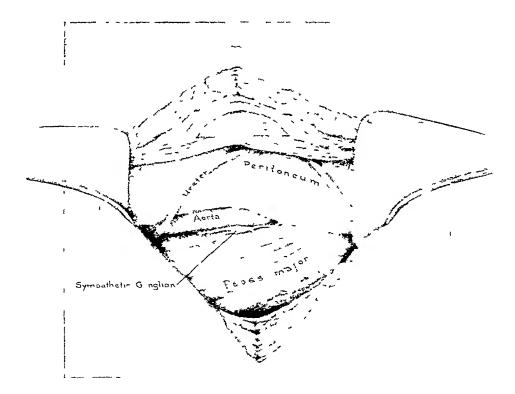
FIG 289 —Exposure of the lumbar sympathetic chain on the inner margin of the psoas muscle

On the inner margin of the psoas muscle the lumbar trunk is first identified by palpation. It rolls beneath the finger like a firm cord. The fascia over it is opened with scissors, and the trunk caught up on a hook. It is then easy to separate its connections one by one and free it from the point where it emerges between the crura of the diaphragm to the point where it disappears into the pelvis. It is cut off above and below and completely removed. In our experience the simple ramisection still advocated by Royle is less permanent in its results than is complete removal of the chain. Some care must be exercised with the lumbar arteries and veins. If the lumbar sympathetic chain lies in front of the vessels, its removal gives no trouble, but if it lies posterior to them, it must be freed and drawn out from beneath them without sectioning the vessels. If this is done, there will be no trouble from hæmorrhage.

Removal of both lumbar chains at one sitting is quite easily and safely performed by this method.

The wound is then closed in layers, muscle by muscle, care being taken to suture the fascial covering of the muscles rather than the muscles themselves.
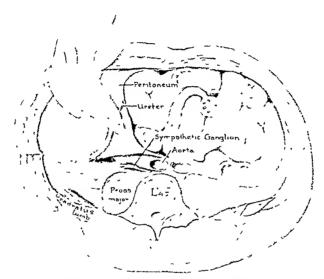
FIG. 290 —A diagrammatic transverse section indicating the approach to the lumbar sympathetic chain.

A very excellent repair of the abdominal wall is thus obtained, and healing occurs without weakness.

Stellate Ganglionectomy.—For the removal of the stellate ganglion, the posterior approach first advocated by Henry[1] is much better than the anterior approach. The technical modification devised by White[2] is excellent and readily permits the removal of both ganglia at one sitting. The illustrations in White's article are confusing because of a most unfortunate typographical error which has separated the titles from the illustrations to which they belong and has placed them beneath illustrations to which they do not refer. By White's transverse incision the operation becomes entirely a muscle-splitting approach and is nearly avascular. Exposure is relatively simple and the stellate ganglia readily removed.

SUMMARY AND CONCLUSIONS

1. Removal of the lumbar sympathetic chain or the stellate ganglion interrupts the vasoconstrictor fibres to the lower and upper extremities respectively and results in profound and lasting increase in blood-flow. Ramisection as distinct from ganglionectomy is less certain and less permanent in its results and should be abandoned in favour of ganglionectomy.

2. The element of vasospasm is present in all of the common vascular diseases

even where the basic pathology of the disease is obliterative. The degree of vasospasm is capable of being determined by temporary block of the sympathetic nerves with novocain.

3. In appropriately selected cases of vascular disease (i.e., those in which a demonstrable degree of vasospasm exists) sympathetic ganglionectomy will result in great improvement in the circulation of the involved extremity. This improvement may be so great as to amount to a symptomatic cure and in any case results in considerable alleviation of the disease.

4. The operations of choice are the transverse abdominal incision for the removal of the lumbar chain and the posterior transverse incision of White for the removal of the stellate ganglia.

My thanks are due to Prof. W. E. Gallie for permission to report these cases from the records of the surgical service of the Toronto General Hospital, and to Dr. J. A. MacFarlane and Dr. D. W. G. Murray who with the author were the surgeons operating upon the cases reported.

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THE PERIPHERAL SYMPATHETIC NERVOUS SYSTEM

By H. H. WOOLLARD

UNIVERSITY PROFESSOR OF ANATOMY, ST. BARTHOLOMEW'S HOSPITAL

SINCE the surgery of the sympathetic nervous system of necessity consists in the removal of certain portions of it, the problems directly concerning the surgeon can be reduced to two—namely, where best can these excisions be performed, and what results may be expected from such excisions ?   Three places may be regarded as the ones likely to continue to be chosen : (1) The region of the stellate ganglion ; (2) The abdominal sympathetic chain ; (3) The hypogastric plexus with or without the inferior mesenteric ganglion.   All these procedures interrupt pre-ganglionic fibres, remove ganglion cells, and with these of course the post-ganglionic fibres to which they give origin.   From the point of view of the physiological effects interruption or removal of any one of these three would achieve the same results.

The ganglionic regions are chosen because they are places where the sympathetic innervation for considerable regions of the body is gathered into a narrow area, i.e., they may be considered as nodal points, and further the removal of the ganglion cells makes regeneration impossible.

The Stellate Ganglion.—Excision of the stellate ganglion will bring about a sympathetic denervation of the head and face on the corresponding side and cause the mildly unsightly picture of Horner's syndrome from palsy of the unstriped muscle of the orbit—the narrowing of the palpebral fissure, the constriction of the pupil, and the apparent but not real enophthalmos.   I have read that some surgeons sensitive to æsthetic considerations have proposed a bilateral operation to get rid of this defect by having both eyes in the same condition.

Effects on the glands of the head and neck region can be ignored, and the absence of sweating and goose flesh are of no importance.

The cardio-accelerators will be interrupted, and again this effect seems to be of no importance to the well-being of the patient.   (Some fibres to the thoracic viscera, such as the lungs and œsophagus, will be interrupted.)

The upper extremity will be deprived of its sympathetic innervation.   This will affect sweating and the goose-skin reaction, but these can be ignored.   The vasoconstrictors to the upper extremity will be interrupted, and this is the important effect that needs further discussion.

The Vasomotor System.—Investigations on the vasomotor system are very difficult because of the many factors involved.   There is the physical fact that blood is an incompressible fluid and must go somewhere.   There are nervous factors, compensatory factors such as local and general reflexes, the liberation of adrenalin by the suprarenal medulla, and the inherent properties of unstriped muscle.

The effects of the sympathetic system are of two kinds—those which are episodic like the pilomotor or goose-skin reaction and the sweating ; and those

which are continuous and tonic. The latter class includes the vasoconstrictor effect.

Concerned in the regulation of blood-pressure there are reflexes which seem purely regulative like the aortic nerve (the depressor) and the carotid nerve (the sinus reflexes—glossopharyngeal), the object of which is to keep the blood-supply to the brain constant. These must be reckoned with in the interpretation of vascular experiments.

The tonic constrictor supply by the sympathetic is the only continuously active pressor system that is known, and if the experimental researches on spinal anæsthesia in dogs are to be trusted, something like 50 per cent of the normal blood-pressure is dependent on these pressor impulses. This fall can be largely counteracted if ephedrine be administered before the spinal anæsthesia is induced. These pressor influences pervade the whole body, with the possible exceptions of the heart, where they exert a dilator effect ; the brain, where the constrictor effect is mild or absent ; and the lungs, where again the effect is slight if present. The pressor effect includes all the trunk and the abdominal viscera, and again, if the results of anæsthetizing the sympathetic rami as they leave the cord by the ventral roots are reliable, the splanchnic area is not more important than the trunk or limbs from the point of view of the pressor result. That is to say, the older ideas of the splanchnic pool into which all the blood of the body could easily drain have been somewhat exaggerated. It is, I understand, a common observation that surgeons operating with the aid of spinal anæsthesia are not incommoded by any unusual engorgement of the viscera. Further observations on this point by those who have the opportunity would be interesting.

Vasodilators.—Vasodilators are much less well understood. They include some special nerves like the chorda tympani and the cranial parasympathetic in general, the pelvic nerves, or the nervi erigentes or sacral parasympathetics ; possibly the ordinary spinal nerves, the antidromic vasodilators (or they may be special vasodilator nerves issuing by the dorsal roots) ; and finally there is evidence in most parts of the body of some vasodilators which belong to the grey rami of the sympathetic. These, however, are overshadowed by the vasoconstrictor fibres present in these same rami.

The surgical excision, then, removes a portion of this tonic constrictor effect of the sympathetic—an effect which can be shown to be permanent though its maximal dilator level becomes subdued presumably by the tone which is inherent in the unstriped muscle of the blood-vessels. Thus sympathectomy gives us in some degree a permanent vascular dilatation in the denervated area. The application of this result is continually being extended, as, for example, to infantile palsy by Telford and Stopford. It is the only effect that seems to be of any value in the limbs. This statement in regard to pain may need some qualification.

Clearly it becomes of importance to be certain how far the vessels can respond to this release from constrictor tonus. Many ways have been elaborated for doing this, but reference will be made to one only.

For some time we have been studying the peripheral vessels in amputated limbs by means of barium injections and X-ray pictures. This has revealed some interesting points. It discloses in the limbs a whole series of arterial anastomoses amongst the smaller arteries. It gives a picture of the relative density of the arteriolar bed, and shows how enormously richer this is in the plantar region.

It gives in the outline of the vessel wall and in the calibre of the vessels an idea of the nature and distribution of structural changes. Such a method applied in the living would be a means of detecting the presence, the nature, and extent of the structural changes in the vessels, and would thus help to distinguish between spasm and organic disease and also would be of use in determining the level of amputation so that this might be a true elective site and not a rule of thumb. It is clear from the literature that the recent methods of investigation of the circulation in the limbs has encouraged a much more conservative attitude in regard to amputation in general and also of the site at which it may be performed.

Thorotrast is the substance which has been used in the surgical unit at St. Bartholomew's Hospital and some interesting results have been already obtained.

Differences between the Upper and Lower Limbs.—Surgeons have frequently drawn attention to the fact that a sympathectomy for the lower extremity—a lumbar ganglionectomy—is often much more satisfactory than a similar operation for the upper extremity. It has frequently been suggested that the explanation of this lies in anatomical differences of the sympathetic chain, and there has been a tendency to urge the removal of more and more thoracic ganglia as well as of the stellate (inferior cervical ganglion and 1st thoracic ganglion). By various anatomical methods it has been shown that there is a greater abundance of sympathetic fibres to blood-vessels at the distal member of the extremities and these parts have also a greater richness of the arterial bed. These facts explain why angiospasm should be most noticeable in the distal members of the limb. The anæsthetization of nerves reveals that the greatest release from constrictor tonus occurs in the hands and feet, and the same method also shows that the foot increases its temperature to almost twice that of the hand. This suggests that the degree of constrictor tonus is much higher in the lower extremity than in the upper. Further evidence of this increased constrictor tonus is shown in the fact that a person lying horizontal in a warm room will show peripheral skin temperatures highest in the face region, next highest in the upper extremity, and lowest in the feet. If the legs are plunged into hot water, the upper limbs will quickly show an increased skin temperature, while the reverse experiment—plunging the arms into hot water—takes a very much longer time to increase the temperature of the legs, and sometimes the effect of the warming does not appear in the legs.

It is clear that the upright posture demands an increased constrictor tonus in the lower extremity if the effects of gravity are to be counteracted.

Thus I think the better expectations of a good result from sympathectomy in the lower extremity are to be explained by the higher constrictor tonus of this extremity.

The Viscera.—For surgical purposes one acts on the general law that the sympathetic inhibits the onward peristaltic wave of the viscera and at the same time increases the activity of the sphincters, the vagus and the pelvic nerves having the opposite effects. This is an over-simplification of the problem, for the results of all animal experiments concur in suggesting that the antagonism between the two systems is nothing like so sharp, that both systems can sometimes act either as augmentors or inhibitors, and that the action which occurs depends on the tonus of the gut muscle at the moment of the inquiry, and this tonus depends

perhaps on the intrinsic nerves of the gut which extend from the lower œsophagus to the rectum, and on other factors not yet elucidated.

In the present state of knowledge it is not profitable to discuss this matter further, but it must be remembered by the surgeon that the issue of sympathectomy in the viscera is not by any means clear-cut.

The Œsophagus.—The œsophagus contains much striate muscle and there is agreement about the importance of the extrinsic nerves and the medullary centre for deglutition.

The lower third is non-striate, possesses an intrinsic nerve plexus, participates in the movements of the stomach such as those of hunger contractions, and varies
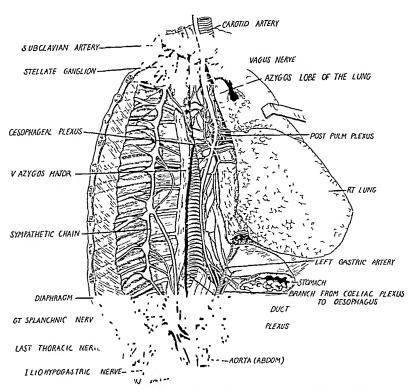
FIG 291 —Dissection of the nerves to the œsophagus in a human fœtus   Right side

much in tonus, being closed when the stomach is full and relaxed when the stomach is empty.   Augmentor and inhibitor fibres have been found in both the vagus and sympathetic.

The vagal plexus closely invests the lower two-thirds of the œsophagus and numerous twigs from this plexus can be seen to enter its muscular walls.   Slender sympathetic filaments from the inferior cervical and thoracic sympathetic ganglia travel alongside the intercostal vessels, but they are too small and delicate to trace beyond the front of the vertebral column and the aorta.   It seems unlikely that the œsophagus receives other than a very scanty sympathetic supply directly from the adjacent ganglia (*Figs.* 291, 292).

Sympathetic fibres, however, do reach the œsophagus from above, having entered the vagi from the cervical sympathetic chain. The other route by which sympathetic fibres may reach the region of the cardia is by way of the cœliac plexus, from which they may travel in company with the left gastric artery. The sympathetic fibres which come from above could be conveniently interrupted by removal of the stellate ganglion.

Knight, in his experimental work on cats, was led to emphasize the importance of this cœliac contribution as inhibitor of the cardiac sphincter and suggested its removal for cardiospasm.

The Colon.—For our knowledge of the neurosurgery of the colon and bladder we are mainly indebted to Professor Learmonth. He has suggested that the
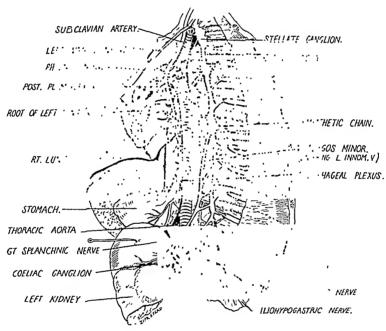
FIG. 292.—Dissection of the nerves to the œsophagus in a human fœtus. Left side.

association of bladder disturbances with megacolon implies that this common embryological unit innervated from the same neural sources must be reacting to some common underlying cause.

It should be pointed out, as Learmonth has done in his papers, that the internal generative organs receive their nerves from the hypogastric plexus, and that, despite many suggestions to the contrary, no clear evidence has been produced that these organs receive any parasympathetic fibres. Their glandular activity and muscular contractions are activated through the sympathetic, and when denervated, as they are by removal of the hypogastric plexus, in the male at any rate the seminal fluid becomes imperfect and sterility may follow.

The Kidney and Ureters.—The kidney may perhaps receive some fibres from the vagus. If it does, no evidence has been obtained that they have any

function.   It is supplied by efferent sympathetic fibres which proceed along the renal vessels from the renal ganglion and from the adjacent aortic plexus.   These sympathetic fibres are apparently purely vasomotor in function.   No clear evidence has been obtained of secretory fibres, and the temporary diuresis that follows a sympathectomy is best explained as the result of vasodilatation.

The movements of the ureter are poorly understood.   Unlike the case of the œsophagus the evidence for nervous regulation has hitherto been regarded as very slight.   Both peristalsis and anti-peristalsis are easily elicited by direct stimulation. The nerves are derived from the renal plexus and from the spermatic plexus, but these contributions seem extremely scanty.   To the lower portion of the ureter they come from the hypogastric and from the pelvic nerves, and these seem abun-dant.   Just as the œsophagus gives the impression of carrying its nerves downwards with it, so the ureter gives the impression of carrying its nerves upwards with it.

To the idea that the ureteric movements were myogenic in origin it has been added that the control of its lower end was purely mechanical owing to its oblique course through the bladder musculature.   However, Learmonth has brought the first convincing evidence that its lower end is strongly contracted by stimulating the hypogastric nerve.   Hence it falls into line with the behaviour of the colon, and removal of the hypogastrics should help in the condition of the megalo-ureter.

The Distribution of the Pelvic Nerve.—It has always been a problem to what extent the colon is innervated by the pelvic parasympathetic nerves. If, as most physiology text-books suggest, the vagus ceases at the ileocolic sphincter, then it might be supposed that the innervation of the whole of the colon came via the pelvic parasympathetic nerves (pelvic nerves).   It would seem almost an anatomical impossibility that this should be so.   If the vagus be taken as far as the splenic flexure, the difficulty, though less, is still great.   The belief that the pelvic parasympathetics do reach the colon depends on the effects of stimulation, for then a contraction of the rectum and the colon occurs.   How much of the colon contracts is not clear.   It has been suggested by some anatomists that the pelvic nerve-fibres get to the colon by ascending in the hypogastric plexus, and if this is so, then removal of the hypogastric plexus should denervate the bowel and this should invalidate the good effects of sympathectomy for megalocolon. Anatomical work done by Mitchell at the suggestion of Learmonth does not support such a contention.   My own dissections are in agreement with Mitchell and do show some fibres which appear to ascend from the pelvic nerves, but the largest of these pass upwards near to, but not actually in contact with, the superior hæmorrhoidal artery, and if they are pelvic fibres they would not be included in the removal of the hypogastric plexus.   Division of the pelvic nerve in the cat shows no degenerated fibres in the hypogastric nerves. (*Fig.* 293.)

It is of interest that evacuation of the bowel occurs after spinal anæsthesia. Since the sympathetic system and pelvic nerves are out of action, it may be inferred that the vagus alone is operative.

At the moment I am inclined to follow the French anatomists who would extend the influence of the vagus as far as the limit of the colon and confine the pelvic nerve to the pelvis.   In fact they call it the ano-perineal nerve.   It seems at present that we may ignore the possibility of denervating the colon entirely by removal of the hypogastric plexus.

Afferent Fibres.—There is still in my opinion no reason for departing from the statement of Langley that the afferent fibres which run with the sympathetic system are visceral afferents coming from dorsal roots and spinal ganglia like sensory nerves.

Despite some suggestions to the contrary, there is no reason to suppose that the rami to the limbs or the cervical sympathetic chain contain any afferent fibres. Blood-vessels in the limbs receive an abundant sensory supply, but anatomy and experiment show that these are fed to the vessels from the adjacent nerves. The alleviation of some kinds of pain by sympathectomy are not to be explained at all by interruption of afferent fibres. The explanation of the good results reported is unknown to me.
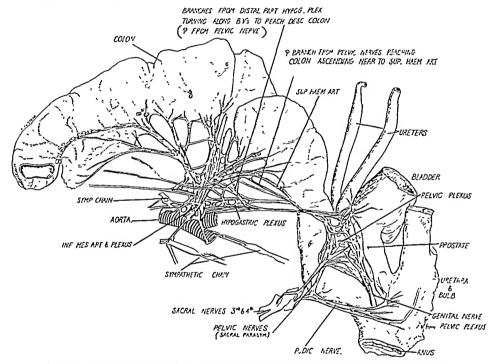
FIG. 293.—Dissection of the inferior mesenteric, hypogastric, and pelvic nerves in a human fœtus. The apparent ascending course of branches of the pelvic nerves is indicated.

In the case of the viscera the afferents do run with the sympathetic fibres. They enter the white rami, connect with the spinal ganglia, and enter the cord by the dorsal roots.

For the heart the upper four dorsal roots and ganglia furnish the pathway of cardiac afferents. They can be interrupted at the stellate ganglion, at the spinal ganglia, or in the roots. Cardiologists are coming more and more to regard the pain in angina as the symptom to be relieved, and if the pain can be abolished such patients go on very well for a long time. It is not so much a danger signal as a thing to be got rid of. If this is so, it is clear some form of surgical section or injection is indicated if drugs fail.

The great splanchnic contains a large number of afferents and is the high-way of sensory impulses from the viscera of the upper abdomen. The kidney receives its afferent fibres via the lesser splanchnic, which, according to some observers, is an entirely afferent nerve. Afferent endings are known anatomically in the perinephric tissues, in the capsule of the kidney, in the renal sinus, and about the pelvis. Renal pain in hydronephrosis of non-obstructive origin should be alleviated by injection or section of the lesser splanchnic.

The hypogastric plexus conducts many afferent fibres from the pelvic viscera and this fact has been made use of for the alleviation of a variety of painful affec-tions of the pelvic viscera. The pelvic nerve also contains a large number of afferent fibres, but these subserve so many important reflex functions that even if they were accessible they are better left alone.

It would not be proper to end these few observations without referring to the brilliant work recently accomplished at the Medical Research Institute by Sir Henry Dale and his co-workers. Their results abolish the terms used in the course of my remarks—indeed, they abolish the very title of the paper, for it is now known certainly that a portion of the cerebrospinal nervous system and the whole of the autonomic nervous system achieve their effects through the inter-mediation of chemical substances. These substances normally formed in the body are acetyl-choline and adrenalin. Thus there are two kinds of nerves which are to be called cholinergic and adrenergic :—

The cholinergic system includes : (1) The pre-ganglionic and post-ganglionic fibres of the parasympathetic system; (2) The pre-ganglionic system of the sympathetic; (3) Some post-ganglionic fibres of the sympathetic system such as the fibres of the sweat glands, possibly the vasodilators, and some of the fibres to the gut; (4) The ordinary motor fibres to the striate muscles.

The adrenergic fibres comprise the remaining post-ganglionic fibres of the sympathetic nervous system.

This grouping cuts right across the existing classification. Already this discovery of the chemical intermediation of nervous processes has cleared up the difficulty about sweating, always anomalous in its pharmacology. Doubtless it will make clear much of the contradictory actions of the autonomic fibre on the gut muscle and sphincters.

THE RESULTS OF SYMPATHECTOMY

AN ANALYSIS OF THE CASES REPORTED BY FELLOWS OF THE ASSOCIATION OF SURGEONS *

By J. PATERSON ROSS

ASSISTANT SURGEON AND ASSISTANT DIRECTOR OF THE SURGICAL PROFESSORIAL UNIT, ST. BARTHOLOMEW'S HOSPITAL

THE Association of Surgeons is greatly indebted to those Fellows who submitted their case records for analysis, but it is regrettable that the total number of these records is less than 250, and that nearly half the cases have been reported on within a year of operation. Only about a quarter of the cases have been followed up for long enough to show the *late* results of sympathectomy, and in order to make this matter as clear as possible the analysis has been made so as to indicate the results at stated periods after operation.

I. DISORDERS OF THE CIRCULATION

1. Sympathetic Ganglionectomy for Raynaud's Disease.—

Severity of the Disease.—When the clinical notes of the cases of Raynaud's disease were scrutinized it soon became apparent that they fell into three groups according to their severity, and that, at all events in the upper extremity, the result of operation varied with the severity of the disease. In the mildest cases exposure to cold gave rise to uncomplicated attacks of cyanosis, but when the disease was moderately severe shallow ulceration of the finger-tips occurred and pain was a more prominent feature, being severe enough in many cases to interfere with the patient's occupation. The most serious complication, however, was scleroderma, for those who manifested this condition suffered not only from extremely frequent and painful attacks induced by cold and accompanied by ulceration of the finger-tips, but the skin of their fingers became so tightly stretched and stiff that serious crippling resulted in many instances.

Sex Incidence.—Of 41 patients in whom the hands were affected 37 were women, and though the female preponderance was not so well marked when the feet were involved, only 4 of the 20 reported cases were males.

Operation.—Peri-arterial neurectomy is not considered a suitable procedure for the treatment of Raynaud's disease, and only those cases in which there was satisfactory evidence that the inferior cervical and upper two thoracic ganglia, or the 2nd, 3rd, and 4th lumbar ganglia, had been excised were accepted for analysis. The operation results are summarized in *Table I.*

Table I.—Results of Ganglionectomy in Raynaud's Disease

Part Affected	Severity of Disease	Number of Cases	Followed Up For								
			1 Year			2 Years			Over 2 Years		
			Success	Improvement	Failure	Success	Improvement	Failure	Success	Improvement	Failure
Hands	Uncomplicated attacks	21	13			4			4		
	Complicated by ulceration ..	9	4	1		2	1		1		
	Complicated by scleroderma	11			3	1				2	5
Feet	Uncomplicated attacks	18	3			7			8		
	Complicated by ulceration ..	2								1	1
	Complicated by scleroderma	0									

The result has been expressed as 'success', 'improvement', or 'failure', but it is necessary to define more accurately what these terms imply. By success must be understood a great diminution in the frequency and severity of attacks, but not complete absence of attacks. In all cases conforming to the accepted criteria of Raynaud's disease exposure to cold gave rise to cyanosis even after sympathectomy. Recurrences have been observed particularly in the hands, and if the cyanosis was less easily induced and was unaccompanied by pain, the operation has been regarded as successful.

A few cases could not be regarded as successful because ulceration had recurred after operation, but since pain had been abolished the result has been considered an improvement. Patients in this group who before operation were prevented by pain from carrying out even the simplest household duties were subsequently able to undertake work involving exposure to fairly intense cold without suffering for it.

When pain, which was usually distressingly severe, accompanied the recurrence of cyanosis and ulceration the patients were unable to work, they were obliged to protect their hands from exposure even to moderate chilling, and the operation

had not only failed to ameliorate their symptoms but seemed in some cases to have aggravated their discomfort.

Table I shows that operation was successful in all the mild cases of Raynaud's disease and in the majority of those complicated by ulceration, but that when the disease was present in the severe form accompanied by scleroderma sympathectomy was a complete failure in 8 out of 11 cases. It is remarkable that the changes characteristic of scleroderma were not present in the feet in any of the cases treated by lumbar ganglionectomy, and this feature may be of significance in accounting for the more favourable results of lumbar as compared with cervico-thoracic ganglionectomy for Raynaud's disease.

2. Sympathetic Ganglionectomy for Obliterative Arteritis.—

a. Thrombo-angiitis Obliterans.—Here again it seemed that the cases could be grouped according to their severity into those in which intermittent claudication was the only prominent symptom, those in which pain was present at rest as well as after exercise, and those complicated by gangrene of the toes.

As regards the incidence of the disease it is noteworthy that out of 69 patients no fewer than 66 were men; and only 3 operations were performed for manifestations of the disease in the upper extremities.

The results of lumbar ganglionectomy in 66 cases of thrombo-angiitis obliterans are given in *Table II*, which includes 46 cases operated upon and followed up by Professor E. D. Telford, to whom we are indebted for valuable assistance and advice.

Table II.—RESULTS OF GANGLIONECTOMY IN THROMBO-ANGIITIS OBLITERANS

SEVERITY OF DISEASE	NUMBER OF CASES	RESULT					
		Claudication		Rest-pain		Gangrene	
		Diminished	Persisting	Relieved	Persisting	Arrested	Major Amputation
Claudication only	29	19	10				
Complicated by rest-pain ..	15			12	3		
Complicated by gangrene of toes	22					14	8

Table II confirms the prevalent impression that intermittent claudication is a symptom which is difficult to relieve by operation. Rest-pain, however, and early gangrene often respond to ganglionectomy in a manner which is most gratifying considering that the disease tends to be progressive, and that high amputation is frequently the only alternative method of treatment. When gangrene of a toe is established sympathectomy may be regarded as successful if the patient loses his toe instead of losing his leg.

The study of these cases has failed to indicate any clinical features by which one can forecast the result of operation. The response of the skin temperature

to spinal anæsthesia is sometimes helpful, but a poor response must not be regarded as a clear contra-indication to ganglionectomy. It may be that further experience with arteriography will point the way to the solution of the problem.

The beneficial effects of sympathectomy seem to depend upon the possibility of improvement in the peripheral circulation resulting from dilatation of vessels as yet unaffected by the disease, and it is questionable whether the pathological process itself is retarded by the operation. There is no doubt, however, that serious complications of the disease can appear very shortly after operation, and in at least two of the reported cases amputation had to be undertaken because of thrombosis of the diseased popliteal artery, which took place within a week of the patient's discharge from hospital, and well within the period during which the post-operative vasodilatation might be expected to be fully developed.

The 3 patients who suffered from thrombo-angiitis obliterans involving the arms were treated by cervico-thoracic ganglionectomy, the operation being successful in 2, but a complete failure in the third.

b. Other Forms of Obliterative Arteritis.—Lumbar ganglionectomy proved to be of no value in one case of syphilitic endarteritis. Three cases were reported in which lumbar ganglionectomy was performed for senile arteriosclerosis. One patient obtained relief from rest-pain, and in the other two, though amputation became inevitable, the legs were taken off below the knee and the stumps healed well.

There were no cases of diabetic gangrene treated by ganglionectomy ; reference will be made later to the value of peri-arterial neurectomy in senile and diabetic gangrene.

3. Sympathetic Ganglionectomy for the Circulatory Disorders following Infantile Paralysis.—One case was reported in which cervico-thoracic ganglionectomy had been performed without success for ulceration of the hand following infantile paralysis, whereas there were 26 cases of impaired circulation in the legs treated by lumbar ganglionectomy.

Table III.—Results of Ganglionectomy for the Circulatory Disorders following Infantile Paralysis

SEVERITY OF DISEASE	NUMBER OF CASES	FOLLOWED UP FOR								
		1 Year			2 Years			Over 2 Years		
		Success	Improvement	Failure	Success	Improvement	Failure	Success	Improvement	Failure
Legs cold and blue ..	9	5		1	3					
Legs cold, blue and ulcerated	17	7	1	1	2	1	1	4		

It is stated that in acute anterior poliomyelitis males and females are attacked with equal frequency, and it is therefore interesting to find that in this series

there were nearly four times as many girls as boys suffering from cold blue legs as a late complication of the disease. Furthermore the circulatory phenomena observed were as a rule less severe in the males than in the females.

In *Table III* the cases have been divided into those in which the affected limb was merely cold and cyanosed, and those in which the presence of ulceration indicated a more severe degree of circulatory embarrassment. The results were distinctly encouraging, both the colour and the temperature of the affected limbs being restored nearly to the normal state, and on the whole they were better in the cases without ulceration. The only failure in the milder group occurred in a girl of 19 whose leg had to be amputated for pain less than a year after lumbar ganglionectomy had been performed in the hope of relieving this symptom.

In the group with ulceration of the legs 13 were successfully treated; 2 operations resulted in improvement, the 'chilblains' being much less severe though still present; and 2 were failures, with persistent ulceration in one case, and pain necessitating amputation in the other.

One instructive case was reported in which lumbar ganglionectomy had been performed for 'trophic' ulceration of the leg complicating spina bifida. The ulcers were situated on an anæsthetic area of skin, and the operation had no effect upon them.

4. Lumbar Ganglionectomy for Erythrocyanosis Frigida.—This condition affecting the legs of young women was also divisible into two groups, one in which the skin showed only the characteristic patches of mottled red and blue discoloration, and the other in which ulceration had supervened. The results of operation are shown in *Table IV*.

Table IV.—RESULTS OF GANGLIONECTOMY IN ERYTHROCYANOSIS FRIGIDA

SEVERITY OF DISEASE	NUMBER OF CASES	FOLLOWED UP FOR					
		1 Year		2 Years		Over 2 Years	
		Success	Failure	Success	Failure	Success	Failure
Legs cold and blue	10	1		4		5	
Legs cold, blue, and ulcerated	4	2			2		

After operation the legs became warm and pink in all the uncomplicated cases, but 2 of those with ulcers suffered from recurrent ulceration, though there were no signs of restoration of function in the structures supplied by the sympathetic.

The thickening of the tissues which is often associated with erythrocyanosis frigida and is commonly referred to as 'œdema' was noted to be diminished after operation, but, though the subcutaneous tissue may have felt softer, the limb seldom recovered its natural shape.

II. DISORDERS OF THE COLON

1. Sympathectomy for Idiopathic Dilatation of the Colon (*Hirschsprung's Disease*).—The most striking feature in the reports of these cases was the variety of operations undertaken for its relief, which indicates the lack of agreement as to the best method of blocking sympathetic impulses to the bowel without damage to the parasympathetic supply. There were 29 cases reported in children, and as constipation and distension of the abdomen had been present since birth, the term 'congenital megacolon' would be a suitable synonym for this group.

Sex Incidence.—It is noteworthy that of the 29 patients 17 were boys, and since this sex incidence presents a striking contrast to that of intestinal stasis in adults, in which there is a well-marked female preponderance, it is an argument against the view that stasis in adults is merely a late manifestation of a defect which has been present in a latent form since childhood.

Table V.—RESULTS OF OPERATION IN HIRSCHSPRUNG'S DISEASE

OPERATION	NUMBER OF CASES	FOLLOWED UP FOR								
		1 Year			2 Years			Over 2 Years		
		Success	Improvement	Failure	Success	Improvement	Failure	Success	Improvement	Failure
Inferior mesenteric and pre-sacral neurectomy	17	8	1		4			3	1	
Bilateral lumbar ganglionectomy	9		1	1	1	2		4		
Left lumbar ganglionectomy	2		1		1					
Presacral neurectomy	1		1							

The results of operation are shown in *Table V*. Seeing that before operation none of these children had ever had a spontaneous action of the bowels, most of them required enemata at regular intervals, and many had suffered from repeated attacks of fæcal impaction with complete intestinal obstruction, the success achieved in 21 out of the 29 cases was dramatic. Enemata were never required, and, though an aperient might have to be given occasionally, the bowels acted as a rule without help. The general condition of the patients showed a remarkable improvement, which was especially noticeable in their colour, growth, nutrition, and energy.

In the 7 cases in which the operation result is described as 'improvement' aperients were required more frequently, but in only 1 was an occasional enema necessary to keep the bowel clear. The only case in which the operation was a

failure was complicated by severe general debility, and the patient died three months after operation without having shown any sign of improvement.

2. **Sympathectomy for Acquired Intestinal Stasis.**—There were 15 cases in this group, and of these 13 were females. The indications for operation seemed to be less clearly defined than in children, and the records did not mention the performance of any pre-operative tests to determine the cases suitable for sympathectomy. The results of operation are shown in *Table VI*.

Table VI.—RESULTS OF SYMPATHECTOMY IN ACQUIRED INTESTINAL STASIS

OPERATION	NUMBER OF CASES	FOLLOWED UP FOR								
		1 Year			2 Years			Over 2 Years		
		Success	Improvement	Failure	Success	Improvement	Failure	Success	Improvement	Failure
Inferior mesenteric and presacral neurectomy	12	2	1	5	1	2	1			
Bilateral lumbar ganglionectomy	2					1		1		
Presacral neurectomy	1			1						

Of 15 operations 7 ended in failure, the state of the patients 'improved' by operation was less satisfactory than that of the corresponding Hirschsprung group, and there seemed to be a tendency to relapse into severe constipation after an initial period of more regular action of the bowel.

From a comparative study of the Hirschsprung group in children and acquired stasis in adults one formed the impression that dilatation of the bowel was a prominent feature in the cases which responded well to sympathectomy, whereas when mere stasis was present without any considerable dilatation sympathectomy was less likely to succeed.

Bladder Involvement.—Infrequent micturition with over-distension of the bladder and a tendency to retention of urine was associated with constipation in 4 of the reported cases of Hirschsprung's disease, and in 3 cases of acquired intestinal stasis. Detailed information was insufficient to make a reliable estimate of the effect of the operation upon the bladder, but there is no doubt that in some instances normal micturition was established, the patients being conscious of a change in bladder function immediately after operation.

III. SYMPATHECTOMY FOR PAIN

1. **Renal Pain.**—The report on the treatment of renal pain is of value because so many of the patients were examined by a uniform method before and after operation by Mr. J. Bagot Oldham. The selection of cases suitable for sympathectomy involved a careful preliminary investigation, and pain was not

accepted as renal unless a characteristic attack could be induced by distending the renal pelvis with fluid injected through a ureteric catheter. In several cases there was considerable delay in the appearance of dye from the affected side on chromocystoscopy, indicating abnormal function of the renal pelvis or ureter, though the common painful diseases of these structures could be excluded.

The operation performed in every case was peri-arterial neurectomy of the renal artery, and in some the stripped artery was painted with 10 per cent phenol. The results of operation are shown in *Table VII*.

Table VII.—RESULTS OF OPERATION FOR RENAL PAIN

GROUP	NUMBER OF CASES	FOLLOWED UP FOR					
		1 Year		2 Years		Over 2 Years	
		Success	Failure	Success	Failure	Success	Failure
Renal pain ..	11	4	1	3		3	
Renal pain with hydronephrosis	8	1		2		5	
Renal pain with nephroptosis ..	7	2	2	1		2	

In the successful cases relief was obtained after an initial period of forty-eight hours during which there was an exacerbation of the pain, and the secretion of urine was diminished. Later, however, the denervated kidney secreted an abnormally large quantity of dilute urine, and dye appeared in the bladder in the normal time in cases which had previously shown delayed excretion. The renal pelvis could be distended with large quantities of fluid without pain.

Table VII shows that in certain cases pain was accompanied by hydronephrosis or nephroptosis, whereas in others it was the only prominent feature; and further that the failures were manifest within a short period after operation. One of the failures was a case which presented unusual difficulty in diagnosis, and the patient died of acute dilatation of the stomach after an operation in which both the gall-bladder and the right kidney were explored. Both the other failures resulted from erroneous diagnosis, for in the one case the complaint of pain was still made although over-distension of the renal pelvis was painless, and in the other pain persisted even after nephrectomy.

2. **Causalgia.**—The investigation included 9 cases of causalgia following peripheral nerve injury in which the characteristic pain persisted in spite of repeated attempts to relieve it by local operations on the damaged nerve. It must be understood that any removable local stimulus had been dealt with before sympathetic ganglionectomy was undertaken.

In 8 cases the hand was involved, and the only case reported of causalgia in the lower extremity occurred in a below-knee amputation stump, the patient being a war pensioner: 5 out of the 9 patients were men. The results of operation are shown in *Table VIII*.

The relief of pain in the majority of cases was remarkable. 'Improvement' signifies abolition of irradiated pain and vasomotor disturbances, but hyper-æsthesia remained over an area of skin surrounding the original wound. Sympathectomy failed to give relief in one case, and when the arm was amputated for persistent pain the median nerve was found to be adherent to the original scar.

Table VIII.—RESULTS OF OPERATION FOR CAUSALGIA

PART AFFECTED	NUMBER OF CASES	FOLLOWED UP FOR								
		1 Year			2 Years			Over 2 Years		
		Success	Improvement	Failure	Success	Improvement	Failure	Success	Improvement	Failure
Hand	8	3		1				3	1	
Leg ..	1	1								

The leg case was noteworthy because the man had suffered from an ulcerated hyperæsthetic amputation stump for twelve years and had never been able to wear an artificial limb. Pain disappeared immediately after lumbar ganglionectomy, the nutrition of the stump was greatly improved, and within a few weeks the patient was able to walk on an artificial limb.

The most suitable cases for sympathectomy seemed to be those in which the pain was accompanied by vasomotor phenomena such as cyanosis and flushing of the skin, over-sensitivity to changes in temperature, and excessive secretion of sweat, and in which any gross local cause of nerve irritation had been removed.

IV. MISCELLANEOUS CONDITIONS

In addition to the larger groups there were several small groups and some isolated cases which deserve notice.

Chronic Arthritis.—Sympathetic ganglionectomy was performed in 5 cases of chronic arthritis associated with excessive sweating and vasomotor disorders in the affected limb. In 3 patients the arm joints were involved, and 2 of them derived great benefit from the operation. In the other 2 patients arthritis affected the lower limb, and in 1 of them the treatment was successful in relieving pain and restoring function.

Hyperidrosis.—This was successfully treated by sympathetic ganglionectomy in 2 patients, one being a woman who suffered from excessive sweating of the hands, and the other a man the skin of whose feet became so sodden with sweat that he was unable to walk to work. After lumbar ganglionectomy the skin was rapidly restored to its normal texture, he was soon able to resume his normal activities, and he had remained well till the time of reporting two years after operation.

Retinitis Pigmentosa.—Seven cases of this condition were treated by superior cervical ganglionectomy. No improvement occurred in 5; the progress of the disease seemed to be arrested in 1; and in 1 case there appeared to be slight improvement.

Spasmodic Dysmenorrhœa.—Presacral neurectomy for spasmodic dysmenorrhœa had been performed twice, one of the operations being successful; but this treatment failed to give relief in a case of congestive dysmenorrhœa.

Sympathetic ganglionectomy failed to improve the condition of two children suffering from spastic diplegia; and the operation was also a failure in a case of post-encephalitic palsy.

Histological Reports on the Sympathetic Ganglia Excised.—Most of the reports stated that sections of the tissue excised showed normal sympathetic nerve-cells and fibres. Degeneration of the ganglion cells, fibrosis, and lymphocytic infiltration of the interstitial tissue were noted as abnormalities by a few pathologists. Since these features were found in ganglia removed in the treatment of various diseases, even when there was no reason to suppose that the sympathetic system was at fault, it is probable that the changes regarded as evidence of disease in the ganglia were in reality variations in the microscopic characters of healthy ganglionic tissue.

Recovery of Function in Denervated Organs.—When accurate temperature records had been made it was found that limbs tended to cool in the course of some months as the effect of the extreme post-operative vasodilatation was passing off. Patients with Raynaud's disease, even those who had been greatly benefited, said they wished their hands had remained as warm as they had been for the first six months after operation.

Horner's syndrome was observed to become less marked in the course of time, especially in the younger patients, but it never disappeared.

Recovery of sweating was noted very seldom, and when it was observed there was some doubt about the completeness of the sympathectomy. The tendency towards vasoconstriction was noted repeatedly in limbs over which sweating was completely absent, and it is unlikely that the restoration of function in the muscle coat of the arteries indicates regeneration of the severed sympathetic nerves. It is more probable that recovery of function means the acquisition of independent activity, and all the evidence seems to favour the view that the sympathetic system is a regulator of function, and not a prime mover as is the cerebrospinal motor system.

Disabilities following Sympathectomy.—After cervico-thoracic ganglionectomy the disabilities were only temporary in most cases, though a few patients complained that as a permanent result of the operation the skin of the hands had become so dry that it cracked, and roughness of its surface interfered with delicate work such as fine sewing. Within a week of the operation a large number of patients began to suffer from pain in the shoulders and arms, which commonly persisted for about six weeks and then gradually passed off. A few complained of weakness of the eyes which required correction by glasses, and there were a few cases in which stuffiness of the nose was troublesome for a few weeks. Excessive sweating over the trunk was an annoyance to some patients,

and seemed to be rather more likely to occur when the lumbar trunk also had been excised.

After presacral neurectomy male patients, though still potent, became sterile owing to interference with the sympathetic supply to the seminal vesicles and to the bladder neck, and a similar effect was noticed in some cases of bilateral lumbar ganglionectomy, presumably when visceral branches going to the hypogastric plexus originated from the excised portions of the lumbar ganglionated trunks. There seemed to be some evidence that, at all events after lumbar ganglionectomy, sterility might not be permanent.

V. PERI-ARTERIAL NEURECTOMY

It has become fashionable to say that peri-arterial neurectomy should have no place in surgery. This attitude has been adopted largely because of our inability to produce any scientific justification for the operation, but there is no doubt of its practical value in the treatment of indolent ulcers, and in alleviating the pain and limiting the extent of gangrene of the extremities.

Reports were made of 32 cases in which peri-arterial neurectomy had been performed, and the results obtained in 20 cases of gangrene deserve special mention. There were 14 cases of senile gangrene, all occurring in males, and involving the left foot in 10 cases. Peri-arterial neurectomy of the femoral artery relieved the pain in 8 cases, the spread of gangrene was arrested in 7, and in only 7 cases was a major amputation required.

Six cases of diabetic gangrene were reported, the sexes being equally represented. As in the senile variety, the left side was more commonly affected, gangrene occurring in the left foot in 5 out of the 6 cases. Pain was relieved after peri-arterial neurectomy of the femoral artery in every case, the gangrenous process was arrested in 4, and in only 2 was a major amputation necessary. Whatever the explanation may be, there seems to be no doubt that this operation is of real value as a palliative measure in this painful complaint when the only alternative treatment is amputation.

CONCLUSION

Except in certain of the cases in which sympathectomy is carried out for pain, it is not correct to say that any of the operations under consideration can 'cure' a patient. These excisions of sympathetic nerves and ganglia have been designed not to extirpate diseased structures, but to rectify disorders of function in organs whose activity is controlled by sympathetic impulses. The results here recorded are of value in so far as they indicate the particular conditions in which this object may be achieved.

CENTRAL CONTROL OF THE SYMPATHETIC NERVOUS SYSTEM

By JOHN BEATTIE

CONSERVATOR OF THE MUSEUM AND DIRECTOR OF RESEARCH, ROYAL COLLEGE OF SURGEONS OF ENGLAND

EXPERIMENTAL work during the past fifteen years has shown that phenomena similar to those elicited by stimulation of sympathetic and parasympathetic nerves can be obtained by appropriate stimulation of a region of the brain forming the lateral walls and floor of the third ventricle. This region is known as the hypothalamus.

Detailed anatomical studies of this region in mammals, including man, have resulted in the plotting out of well-defined cell groups. These masses of nerve-cells lie in three zones—a mass which lies close to the ependymal lining of the ventricle, several masses lateral to the sub-ependymal group forming the intermediate zone, and a still more lateral mass of cells forming the so-called lateral hypothalamic zone in which there is no clear definition of cell groups. Still more lateral to the lateral hypothalamus are found the medial nuclei of the thalamus.

The differentiation of the cell groups in the sub-ependymal and intermediate zones varies considerably in different species. In a like manner there are considerable differences in the size of the various groups. Whatever the significance of these observations may be, it is quite unknown at present.

A study of the fibre connections of the various cell masses gives some clue to their probable functional significance. Speaking broadly, the cell groups in relation to the optic chiasma, i.e., in the more anterior part of the hypothalamus, send fibres into the hypophysial stalk and thence into the posterior and intermediate lobes of the pituitary body. Numerous fibres are also given off which are seen to pass posteriorly in a dense felt-work of fibres towards the brain-stem, where at least some of them end in the upper medulla. The cell groups which lie close under the ependyma send axons into the same system of descending fibres. These sub-ependymal nerve-cells lie close to a very specialized part of the ependymal epithelium, which, as several workers have suggested, may have either a secretory or an absorptive function. More posteriorly and lying dorsal to the mamillary bodies lies the posterior hypothalamic nucleus whose axons pass posteriorly into the brain-stem.

There is thus evidence for believing that at least three groups of efferent fibres arise from hypothalamic nuclei—one group arising in the supra-optic area of the hypothalamus, apparently innervating the posterior and intermediate lobes of the pituitary gland; a second group from some or all of the same nuclei and which pass into the brain-stem; and the third group from the posterior hypothalamus.

The afferent fibres to these various groups are not yet determined, but there is some experimental evidence which suggests some cortical control of the anterior hypothalamus and thalamic control of the posterior hypothalamus. It is unsafe, however, to presume specific fibre-tracts from the cortex or the thalamus in the present state of our knowledge.

It has been demonstrated by many observers that channels or vessels pass from the anterior lobe of the pituitary gland through the stalk of the infundibulum into the region of the tuber cinereum. Many observers, too, have observed so-called ' colloid bodies' in the posterior lobe and in the stalk. These have been presumed to represent some secretion of the pituitary gland. Again, Cushing claims that there is evidence that pituitary secretion may reach the third ventricle by passing through the ependymal epithelium. The weight of evidence at the moment does suggest that some hypothalamic cells, probably those close to the ependyma, are influenced by chemical substances elaborated in the pituitary. Cushing's experiments on unanæsthetized humans, when he placed pituitary extracts in the ventricular fluid and observed very marked autonomic disturbances, tend to confirm the chemical activation of at least some hypothalamic nuclei.

Experimental work on the hypothalamus has consisted of stimulation of small areas electrically, the production of lesions of varying sizes, and the injection of various substances into the ventricular fluid. Various phenomena have been observed, and it is possible to suggest that there are certain areas which give rise to specific effects differing from those obtained from areas only a few millimetres distant. The difficulty inherent in all stimulation experiments must not be lost sight of—i.e., a stimulation point may be accurately localized by histological means, but the actual physiologically stimulated zone is not necessarily coincident. However, by repeated experiments and stimulation of numerous points it has been possible to form some conclusions about the functions of several areas. The method of studying the effects of lesions does not provide so accurate information. Instead of observing some ' defect' in the functioning of the autonomic nervous system, the effects obtained may be due either to the irritation of the lesion or to the release of some other mechanism. For these reasons the effects of hypothalamic lesions require very careful analysis. The injection method has provided useful information about the pituitary-hypothalamus relationship—but has not assisted in the localization of function within the area.

An analysis of all the available evidence of experimental investigations on the hypothalamus confirms the view that the more posterior nuclei are related to the true sympathetic nervous system, i.e., on stimulation of this area the characteristic phenomena of sympathetic excitation may be observed : (1) Cardiac acceleration ; (2) Vaso-constriction of skin vessels ; (3) Rise in blood-pressure ; (4) Adrenalin secretion ; (5) Pupillo-dilatation, etc. These effects are not obtained on stimulation preceded by section of the hypothalamus at the level of the aqueduct of Sylvius and extending not more than 3 mm. from the middle line on each side. They are also abolished or lessened in magnitude by doses of the barbiturates. Ergotamine also prevents their appearance.

A careful study by Biggart of the condition known as diabetes insipidus has revealed the interesting facts that minute lesions of the nuclei close to the optic chiasma, or ligation of the pituitary stalk or its destruction by tumour formation, or lesions in the tuber cinereum itself, can give rise to the disease. There can be

little doubt then that the hypothalamo-pituitary nerve connections are essential for the production of the anti-diuretic hormone of the pituitary gland in normal amounts. The hormone finds its way into the blood-stream and produces its effects on the kidney directly.

Various workers have shown that stimulation of the more anterior regions of the hypothalamus cause effects similar to those brought about by stimulation either of the vagus or pelvic nerves. Tonus of the stomach and bladder are raised, while the reverse effects are obtained by stimulation of the posterior hypothalamus. Compared with the phenomena obtained by stimulation of the posterior hypothalamus, the effects observed are, as a rule, less marked and are obtained from a more circumscribed area. Stimulation of the more lateral nuclei has shown that both sympathetic and parasympathetic phenomena can be obtained from these cell groups. Owing to the great number of fibres which cross this zone, the localization of any specific function in it is not possible.

One of the most important complications following operative procedures in or near the third ventricle is hyperthermia. There can be no doubt that this is due to some disturbance of the normal activity of the hypothalamus. Animals in which the hypothalamus has been destroyed or which have been decerebrated are unable to maintain a normal temperature unless the environmental temperature is maintained at the same level as the normal body temperature. It is well known that the preservation of the posterior hypothalamus, the mamillary bodies, and the tuber cinereum in an otherwise decerebrated animal prevents any disturbance of the temperature control.

Three explanations of these phenomena are possible: (1) The temperature fall is due to increased heat loss; or (2) The temperature fall is caused by a diminished heat production; or (3) By both factors acting together. The balance of evidence seems to favour the second alternative.

It has been pointed out above that the posterior nuclei of the hypothalamus when stimulated cause an increased adrenalin secretion. Moreover, Schmidt has brought forward evidence which suggests that the perfusion of a muscle with small amounts of adrenalin causes a rise in its temperature. Such small doses of the drug produce dilatation of the muscular vessels simultaneously with constriction of those of the skin (Dale and Richards). Clark has shown that these effects are still present even when pressor effects on the blood-pressure are absent, and Gruber demonstrated that when pressor effects do occur the muscular responses are exaggerated.

It seems legitimate, therefore, to presume that the continuous release of small quantities of adrenalin (which release seems to be under hypothalamic control) is responsible for the production of the heat necessary to maintain body temperature, and, further, that the heat is produced in the muscles of the body. Simultaneous constriction of the skin vessels assists by lessening the surface heat loss. The automatic control of this heat production seems to be effected by the hypothalamus itself, as heating of the blood passing to the hypothalamus results in a fall in body temperature, and localized heating of the same region by small copper coils containing hot water or by minute electric heating elements show that the cells of the posterior hypothalamus are very sensitive to minute changes in temperature.

Clinical hyperthermia is probably due to increase of the normal heat production. The pale dry skin with gradually increasing temperature may be explained

by an increase of adrenalin secretion with or without a parallel rise in the blood-pressure. As the centres which may be over-active are those which are very sensitive to the depressing effects of the barbiturates, it may be worth while to attempt to treat cases of hyperthermia by barbiturates even to the point of deep anæsthesia for short periods.

This very brief summary of the evidence in favour of a central controlling mechanism or mechanisms for the autonomic nervous system would not be complete were one to omit reference to Claude Bernard's famous dictum that " the constancy of the internal environment is a condition of the free life." There is no doubt that without some method of stabilizing our ' milieu intérieure ' the life of free-moving and efficient organisms would be impossible. It seems at present that the hypo-thalamus must be regarded as the necessary controlling mechanism of the autonomic nervous system and perhaps for many of the endocrine glands.

THE TECHNIQUE OF SYMPATHECTOMY

By E. D. TELFORD

SURGEON, ROYAL INFIRMARY, MANCHESTER

THE more customary procedures of sympathectomy to-day are lumbar-cord ganglionectomy, cervico-thoracic-cord ganglionectomy, presacral neurectomy, and perivascular operations on the inferior mesenteric and renal arteries. To these we must add the wide resection of the left gastric artery as now practised for obstructive lesions of the cardia.

I do not propose to take up any time with the technique of these; they are on the whole simple and straightforward and have been very adequately described by many writers. I would only say that I have altered my earlier view on the best approach to the cervico-thoracic ganglion. I was originally an enthusiastic supporter of the posterior incision, but in the course of thirty-five of these operations I became increasingly dissatisfied with the method. Not only is the operation more mutilating, involving a more stormy convalescence, but the exposure of the ganglion is not always good because the root of the first thoracic nerve lies between the operator and his objective. I have recently done all cases by the anterior approach, which, if it be thoroughly practised, is easier and gives an excellent view of the ganglion and its connections.

I wish, rather, to talk of the relation of technique to results. I do not think that any operator who has had sufficient experience of sympathectomy and has followed up his cases for some years can regard the outcome of his work as entirely satisfactory. Whilst the results are on the whole good, sometimes dramatically so, some degree of relapse or partial failure is unfortunately too frequent. This is more especially true of the attempted denervation of the upper limb as practised for Raynaud's disease, acrocyanosis, and allied conditions.

A second point is that our technique to-day is too gross and mutilating. We do not know enough to be able to pick out just that part which we wish to destroy. We are obliged to do too much in order to ensure that we have done enough. A good instance of this is the way in which in denervation of the arm we present the patient with a quite unwanted Horner's syndrome. Animal experiments are here of very doubtful value, and our sympathectomies become actual experiments in human physiology. It is only by variations of technique that we can hope to explore.

What, then, is the relation of technique to success or failure in sympathectomy? In considering this I shall ask a number of questions the answers to which I do not know, but on which I am hopeful that this discussion may throw some light.

Incomplete technique is the obvious explanation of some failures. The surgeon has missed his objective or has merely traumatized the structures, producing a real but temporary result which soon vanishes with recovery from the injury. But relapse can follow the most skilfully executed operations, and we must seek other explanations.

Take, for instance, the striking fact that the results in the legs are consistently better and more complete than they are in the arms. Perhaps some local condition such as difference in normal vascular tone may have something to do with this, but one must ask what the difference is between pre-ganglionic and post-ganglionic section. In lumbar-cord ganglionectomy the section must be largely pre-ganglionic and for the area of sciatic innervation is probably wholly pre-ganglionic; the results here are good. On the other hand, the cervico-thoracic ganglionectomy is post-ganglionic for the arm; the results are often clinically disappointing. I have recently practised a technique which approximates the cervical operation more closely to the lumbar.

The stellate ganglion and upper portion of the thoracic sympathetic cord are exposed by the anterior incision. No attack is made on the ganglion itself. The white rami of the second and third thoracic nerves are divided and the cord itself is crushed and divided below the third thoracic ganglia. It is one of the major difficulties of sympathetic surgery that we know very little about the exact position of the cell-station at which the fibres of any one white ramus may end, but it is evident that a section such as I have described is to a large extent pre-ganglionic. It is too early to appraise the result of this method. It will take at least two years, but the immediate result is in all respects excellent, and Horner's syndrome is not produced.

The notoriously variable anatomy of the autonomic system will explain some failures of technique. D. Sheehan's careful dissections and drawings of twenty-five cervico-thoracic ganglia showed that no two were alike in pattern and that the locale of any given ramus varies within very wide limits. Kuntz's nerve, i.e., the direct contribution from the second thoracic ganglion to the plexus is not likely to escape the experienced operator, but is it not possible that alternative paths may exist? It has been shown that fibres may reach the plexus from the vertebral ganglia; is there any possibility of a route by which pre-ganglionic fibres to this ganglion may escape division?

The question of regeneration as an explanation of relapse must arise. It would appear from the work of various observers that sympathetic fibres have an uncanny power of regeneration even when barriers of fascia and muscle fibre have been interposed. These are, however, animal experiments, and it must be seldom that the opportunity arises to study the question of regeneration in the human subject. I had recently one such opportunity. Two years after I had removed the cervico-thoracic ganglion by the posterior approach, I obtained permission owing to an incomplete result to explore by the anterior route. The exposure was very good and it was possible to show, beyond doubt, that there had been not the slightest attempt at regeneration of the divided thoracic sympathetic cord.

D. J. Williams has demonstrated to me on several occasions in our Surgical Laboratory at Manchester very beautiful specimens of sympathetic cell-stations on the walls of cerebral arteries. This finding obviously raises the question whether similar stations in the peripheral circulation may explain the variable and incomplete results which occur from time to time.

The vexed question of the existence of a spinal parasympathetic supply must also come into the picture. Other muscular tubes are known to have a double supply; is it not possible that a similar arrangement obtains for the arterial wall? Kure and his Japanese collaborators claim evidence that there is such a peripheral

parasympathetic supply, but these views have not met with support from other workers. There exist in the posterior root of a spinal nerve a large number of fibres whose function is as yet unknown. At present one can only say that they may be "spinal parasympathetic" fibres. I believe that the surgeon would welcome this explanation because it would throw light on a number of post-operative clinical problems which remain at present without solution.

It is an every-day observation that the brightly injected and warm limb which follows at once on sympathectomy begins to lose its colour and heat in a few days. In my experience this interval is four to five days for the hand and eight to ten days for the foot. We should learn much if we could truly interpret this change. J. C. White claims that it marks the period after which the denervated vessel becomes hypersensitive to adrenalin. His experiments are brilliant and convincing, and, as White writes in a personal communication, if they are true they are going to make the treatment of Raynaud's disease more difficult than we had imagined.

It is possible that we have not attached sufficient importance to the essential automatism of plain muscle. In the gut, Vivaldes has shown the power of contraction of smooth muscle deprived of all nerve-supply. It is evident that although the autonomic system exerts a control over smooth muscle it is not the prime mover, and we have perhaps expected too much from section of its nerve-supply. Certain clinical observations lead one to think that it is possible that this automatic action comes into play after a period of shock due to the section.

Finally, some failures are, as in all surgical work, due to operating too late. The disease has induced secondary fibrotic changes, of themselves irrecoverable and quite enough to vitiate the results of sympathetic section. For example, the operation is likely to fail in advanced thrombo-angiitis obliterans where the vessels are transformed into fibrous rods, and in some cases of old-standing mega-colon and achalasia of the œsophagus in which the original muscular mechanism has been largely supplanted by fibrous tissue.

These are a few of the questions which call for answer, and they will best be met by prolonged clinical observation on the sympathectomized patient. On the answers will depend the ultimate fate of operations on the autonomic system. My own impression, based on a close clinical observation of 150 cases of cord ganglionectomy during four years, is that, in certain directions, these operations will become one of the established procedures of surgery, but it may be that the ultimate field will be more restricted than that in which we are now working.

EXPERIMENTAL SURGERY

THE EFFECTS OF OBSTRUCTION OF THE URINARY TRACT, WITH PARTICULAR RELATION TO THE FORMATION OF STONES

BY J. GRAY

HENRY LESTER INSTITUTE, SHANGHAI

THAT pathological lesions in the urinary tract are more liable to occur in the presence of an obstruction than in the non-obstructed tract may be said to be almost axiomatic. At the same time they do not seem to be inevitable, and it is not always possible to say which is the primary effect, as in the case of hydronephrosis with stone formation. The following clinical case may be relevant as an illustration of this.

A Chinese patient, aged 30, was admitted for severe hæmaturia following a blow on the back with an iron bar. There was some fullness in the loin and rigidity of the abdominal wall. The diagnosis was ruptured kidney, and he was treated expectantly. A month later, as the urine still contained blood- and pus-cells, his urinary tract was investigated, disclosing the presence of a hydronephrosis and stone formation (*Fig.* 294). It is impossible to say in this case which was the primary factor—namely, did the hydronephrosis precede the stone formation or vice versa, and were either or both present before the injury, or did they develop as a result of it? In view of such considerations it was felt that it would be desirable to investigate the condition of the urinary tract in cases of obstruction, and, further, to see if in experimental obstruction stone formation was liable to occur.

FIG. 294 —Pyelogram showing renal calculi and hydronephrosis.

The obvious experiment was to ligature one ureter in a series of animals so that by this means the condition of the obstructed and unobstructed side could be investigated. This was accordingly carried out, the obstruction in 4 cases being partial and in the rest complete, and in both normal animals and those on a stone-producing diet as described in another article. The results may now be considered :—

Twenty-five rabbits were kept on normal diet with complete obstruction for a period averaging at least three months, but in some cases extending to six months

—no stone stone formation occurred.   Thus there appears to be no tendency to stone formation in complete obstruction, presumably because the renal function is progressively diminishing.

Fifteen rabbits were put on a stone-producing diet (Ca and vitamin D) for a period of three months; stones occurred in 4.   There was none in the normal kidney (*Fig.* 295).   It was particularly noticeable that in no case where complete obstruction was present with extensive hydronephrosis did stones occur, but in the 4 cases where obstruction was slight and the hydronephrosis was not noticeable to the naked eye stones formed in all.   It would appear from this that there is no tendency to stone formation (even on a stone-forming diet) unless a
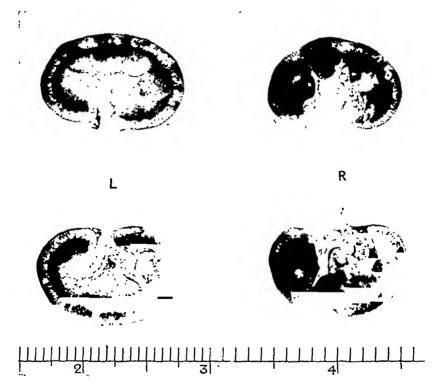
FIG. 295.—Renal calculi—experimental partial obstruction.

considerable degree of kidney function is present.   The urine was examined systematically for pus- and blood-cells.   In a few cases the latter were found, but in no case did the count of the pus-cells exceed 100 per 1 cm., or, in other words, there was no evidence to suggest that infection played any part in the process.

The points investigated were : (1) Renal blood-supply ; (2) Tubular function ; (3) Histology.   These will be considered in order.

1.   **Blood-supply.**—The following methods were used to investigate this : (*a*) Injection of carmine gelatin solution or Berlin blue according to the technique of Hinman and Lee Brown ; (*b*) Arteriography or venography with 100 per cent

sodium iodide (*Fig.* 296); (*c*) Temperature estimations with a thermo-couple; (*d*) Direct measurement of blood-flow by simultaneous bleeding of both renal veins.

The carmine gelatin solution was frequently used after a preliminary two or three injections of intravenous trypan blue. In this way a combined picture showing the tubular function and the vascular supply was obtained. The estimation of the temperature change as a measure of the difference in blood-supply of the two sides was not very convincing, probably because sufficiently sensitive instruments were not available. The other methods need no comment.

All methods used demonstrated a marked diminution in the blood-supply in hydronephrosis.

2. **Tubular Function.**—This was investigated by giving intravital trypan in a dose up to 20 or 30 c.c. spread out over several days. This demonstrated very clearly the dilatation of the tubules and their loss of function (*Figs.* 297, 298).

FIG 296 —Arteriography showing left-sided hydronephrosis

3. **Histology.**—The features investigated were : (*a*) The condition of the pelvic epithelium ; (*b*) The calcium content of the kidney (von Kossa's method) ;

FIG 297 —Intravital trypan blue and carmine gelatin injection of vessels showing normal appearance.

FIG 298 —Intravital trypan blue and carmine gelatin injection of vessels showing effect of hydronephrosis.

(*c*) The presence of mucoid material. The findings in these points may now be considered.

a. The Pelvic Epithelium.—This was investigated by general observation with the hæmatoxylin and eosin stains and also by giving intravital trypan blue
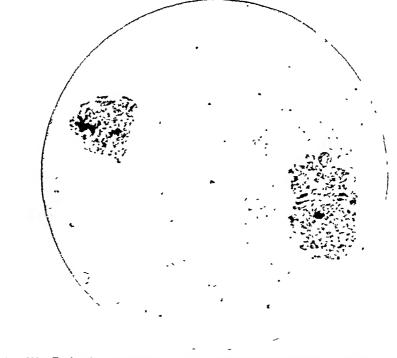
FIG. 299.—Epithelial scraping after intravital stain showing intracellular granules of the dye.

FIG. 300.—Hydronephrosis showing hypertrophy of mucosa and submucosa. (× 168)

and examining scrapings of epithelial cells for granules of the dye. In the case of pathological changes intracellular granules may be seen (*Fig.* 299). This appears, however, to apply only to advanced pathological changes. In the early conditions no definite results were obtained. In the large majority of cases obvious changes in the epithelium were seen. The simplest of these was an irregularity and hypertrophy. In more advanced cases there was a tendency to metaplasia with change to the squamous type, and then desquamation was frequent. At the same time a hypertrophy of the submucosa was also noticed consisting in the laying down of fibrous or fibromuscular tissue. This is well shown in *Fig.* 300.

It can be concluded that severe obstruction, apart from any infection, produces definite pathological changes in the epithelium of the urinary tract.

b. Calcium Deposit.—The findings here were that in the cases of complete obstruction with hydronephrosis there was no tendency to deposition of calcium.
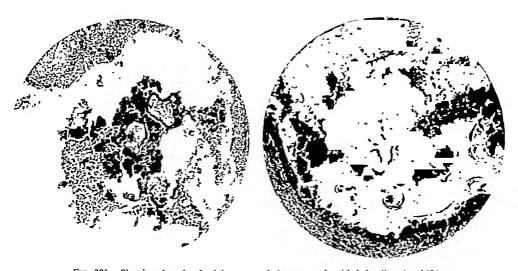
FIG. 301.—Showing deposit of calcium around desquamated epithelial cells. ($\times$ 140.)

This result was unexpected, but can perhaps be explained by the loss of function of the renal tubules. When the obstruction was partial only, then there was a marked tendency to the deposition of calcium and to stone formation. *Fig.* 301 in a partial obstruction shows deposition of calcium around the desquamated epithelial cells, forming a stone. The cause of the increase in calcium deposit is not certain. It may be associated with the decrease in blood-supply according to Leriche and Policard's theory, or it may be due to actual tissue damage and the liberation of fatty acids from which calcium soaps are formed. In the extensive hydronephrosis where tissue damage was great, however, calcium was not found. It was found chiefly in those cases where the damage to parenchyma was not very extensive, and then it was found scattered diffusely through the kidney as well as in the more damaged areas.

c. Mucoid Deposit.—This was strikingly increased as the result of obstruction and can be seen both in the dilated tubules and in the pelvis. *Fig.* 302

illustrates this finding. It is uncertain what relation this may have to stone formation when it occurs. In any case it was most marked in the completely obstructed cases where stone formation did not occur.
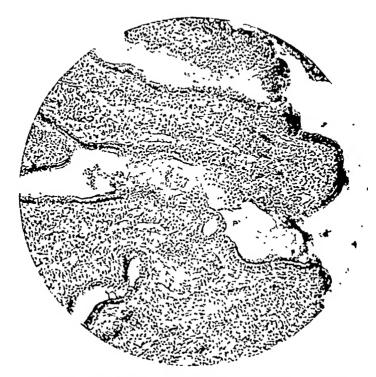
FIG. 302.—Hydronephrosis. Section shows mucin deposit. (× 142.)

SUMMARY

A series of rabbits with unilateral ureteric obstruction has been investigated. The obstruction was in four cases partial and in the others complete, and the period of obstruction varied from a fortnight to six months. It has been shown that a marked effect is produced upon the blood-supply, the renal tubules, and the pelvic epithelium. In addition a number of these rabbits were given a diet which has been found likely to give rise to stone formation. It appears from this that in complete urinary obstruction there is no tendency to stone formation, in partial obstruction there is a marked tendency. The two factors of importance in this seem to be an increased calcium content of the kidney and a pathological condition of the pelvic epithelium, so that calcium may be deposited around this as a nucleus.

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THE EFFECT OF EXPERIMENTAL INTERFERENCE WITH THE BLOOD-SUPPLY OF THE KIDNEYS, WITH PARTICULAR REFERENCE TO THE FORMATION OF STONES

BY J. GRAY

HENRY LESTER INSTITUTE, SHANGHAI

THE basis of these experiments is the theory of Leriche and Policard, which states that deposition of calcium takes place in connective tissue of low metabolism if the blood-supply be diminished, particularly in the presence of hypercalcæmia. Clinically it has frequently been observed that renal calculi may develop in patients who have been recumbent for long periods. This has been noticed particularly in sanatoria for the treatment of bone and joint tuberculosis in children, where recumbency and sunlight are important features in the treatment.

Starting from this point of view, it was felt that if the blood-supply of the kidney were reduced experimentally, in the presence of hypercalcæmia, renal calculi should form. A series of 40 rabbits was used, 20 being on a normal diet and 20 on a diet calculated to produce hypercalcæmia. To effect this, lime (about 2·5 grm. per diem) and concentrated extract of vitamin D (radiostol, 1 drop per diem) were added to the diet. The urinary content of calcium and phosphates was estimated at regular intervals, and regular examination for pus-cells, blood-cells, and albumin was also carried out. It was found that on this diet the urine content of calcium was markedly increased and that of phosphates diminished relatively or absolutely.

With regard to the other part of the experiment, it was at first somewhat difficult to reduce the blood-supply without causing extensive damage to the kidney. However, eventually it was found that, with a little care, it was possible to separate the two terminal branches of the renal artery and ligature one close to the pelvis. When successfully carried out, the effect, noticed in a month or six weeks' time, was to produce a marked diminution in the size of the kidney, with, perhaps, a little scarring but otherwise no change detectable by the naked eye. When the branch ligatured was too large there was obvious necrosis of the renal parenchyma.

The results of these experiments may now be considered :—

DIET	NUMBER USED	STONES FORMED	CALCIFICA-TION
Normal	20	3 (15%)	6 (30%)
Normal, plus calcium and vitamin D ..	20	9 (45%)	5 (23%)

In no case did stones form in the normal kidney. Stones occurred on the ligatured side both on a normal diet and on the calcium-vitamin D diet, but in the latter case the number was three times as great (*Fig.* 303).

The duration of the experiments was about six weeks, although stones were sometimes demonstrable by X-rays in a month or even less. The stones were quite large and were always found in the pelvis or calices, never in the parenchyma.

FIG 303 —Renal calculi

Apart from the regular examination for pus- and blood-cells, whenever possible the urine was cultured at the time the animal was killed. In only an occasional case was there any infection present, and there was nothing to suggest that this played any part at all in the pathology.

The following points were investigated in some if not in all cases : (1) Renal function; (2) Reaction; (3) Histology.

1. **Renal Function.**—This was investigated by giving 5 c.c. of 0·4 per cent indigo blue intravenously and watching the coloration of the kidney and the ureter. It was realized that this is a test of gross defect only, and as a matter of fact no definite difference could be detected in the two sides unless the damage to the kidney was obvious to the naked eye. The experiment was carried out on a dog to check the findings, but with the same result. There was no difference in the time of excretion of the indigo blue and no difference in the concentration of phenolsulphonephthalein. It is concluded that there is no gross defect in renal function as the result of this treatment.

2. **Reaction.**—In some cases both kidneys were split open while the animal was under the anæsthetic and the reaction of the pelvis to litmus paper tested. This was not done in every case as it was found to interfere with the subsequent histology. A sufficient number were examined, however, to demonstrate an obvious alkalinity of the ligatured side, while the normal side was neutral or often acid. In the cases where stones were present the alkalinity was more marked.

3. **Histology.**—The features investigated under this heading were as follows : (*a*) General appearance (hæmatoxylin and eosin) to show the effect of the ligature of a blood-vessel; (*b*) Special stain to demonstrate calcium (von Kossa's method); (*c*) Special stain to demonstrate mucoid material (Mayer's method); (*d*) Special attention was paid to the appearance of the pelvic epithelium in view of the fact that stones formed here—hæmatoxylin and eosin and also intravital trypan blue were used for this; (*e*) Intravital trypan blue was also used as a means of

investigating tubular function; (f) A number of sections of the renal pedicle were made to demonstrate nervous tissue or evidence of nerve degeneration. In all cases the normal kidney was stained in an identical way and examined on the same slide as a control.

In reviewing the findings it seems desirable to consider first the effect of ligature of the vessels, and then to see if any noticeable difference is present in those cases in which stone formation occurred. These points will be considered in order.

a. *General Appearance.*—When the amount of damage was slight, scarcely any detectable difference was present. As, however, the damage became more severe, areas of dilatation or even destruction of tubules could be seen very similar
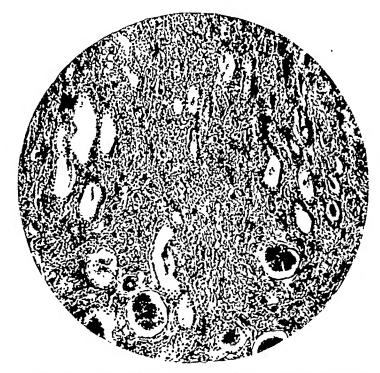
FIG. 304.—Section showing general histological appearance and tubular degeneration.

to the appearance in hydronephrosis (*Fig.* 304). When the damage was very severe an area of destruction was present with severe injury to the tubules, the glomeruli remaining relatively intact. Proceeding away from the most damaged area the tubules were found to be dilated and their epithelial lining hypertrophied. Foreign-body giant cells and areas of hæmorrhage were often seen. There was a marked infiltration with cells.

b. *Calcium Stain.*—As in the previous section, with minor degrees of injury due to deprivation of blood-supply it was not always possible to detect any difference in the calcium deposit in the two sides even though the kidney were definitely smaller to the naked eye. With severer grades of injury the calcium deposit was much more marked, and with very severe grades it was intense even though the

animals were on a normal diet. The calcium was deposited in the areas most damaged (*Fig.* 305).

c. Mucin.—The writer has not been able to find any information as to the formation of mucin in the urinary tract of rabbits and so has been compelled to rely on his own observations made on normal rabbits. It has been difficult to demonstrate mucin with certainty in the bladder, but in the kidney, either in the pelvis or in the tubules (*Fig.* 306), pink-staining material, presumably mucoid, has been demonstrated by means of Mayer's mucicarmine stain. On the whole, following the ligation of vessels the pink-staining material is more commonly found than on the normal side. Too much stress is not laid on these findings, and a bigger series is being undertaken.

A   B
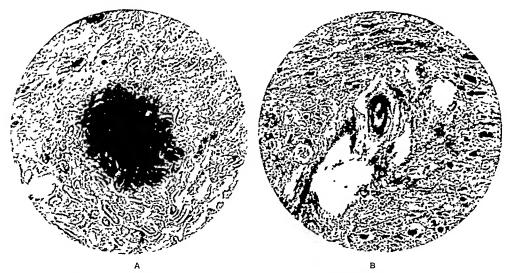
FIG. 305.—Sections showing: A, Calcium deposit; B, Giant-cell formation. (/ 140.)

d. The Pelvic Epithelium.—In view of the observations noted in vitamin A deficiency described in the previous paper, particular attention was paid to this. The difficulty, however, was to be sure what could be regarded as definitely pathological. Unless the changes were gross, therefore, they were disregarded, although after a study of a large number of sections it was often felt that minor anomalies probably did represent early pathological lesions. It was common to notice obvious alteration in the appearance of the epithelium. The changes noted were hypertrophy and irregularity, often with marked desquamation (*Fig.* 307); occasionally areas of metaplasia were to be seen with change to the squamous type, but this was never as marked as in the vitamin-deficient animals. It would seem likely that metaplasia and keratinization represent the final stages of a series of changes which begin with hypertrophy, but that these experiments did not give rise to sufficient damage, or that observations were not carried out over a sufficiently long period to demonstrate the final stage.

In order to confirm the pathological nature of these changes intravital stains were used in 13 cases (a total of 30 c.c. of trypan blue being given intravenously

FIG. 306.—Section to show mucin in the tubules.
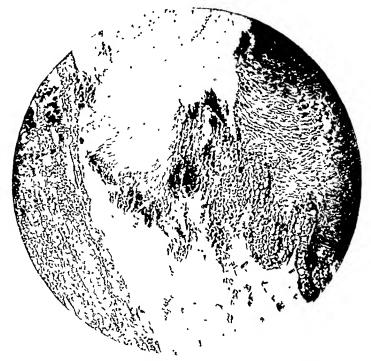
FIG. 307.—Desquamation and stone formation. Oxamide calculi showing epithelial change. ($\times$ 71.)

FIG 308 —Hyaline of branch of renal artery   Stone formation beneath epithelial surface   (╱ 140)

FIG 309 —Showing process of stone formation around the damaged epithelium   (╱ 56)

over a period of several days).   The animals were killed, and a scraping of epithelial cells obtained from the pelvic mucosa was examined fresh, in saline or glycerin, for intracellular granules (*see Fig.* 299, p. 454).   This method was not very convincing, because if the epithelial cells were found to take up the granules (evidence of pathological changes), then the pathological appearance of the epithelium was obvious by ordinary staining methods.   In the lesions which were felt to represent early changes no reliable information was obtained.

e. As a method of examining the tubular function intravital staining proved more useful.   In this case the damaged epithelium failed to show the granules, presumably as it had lost its power of concentrating.   It is noted that this reaction is the reverse of the reaction described in the previous section, where the damaged
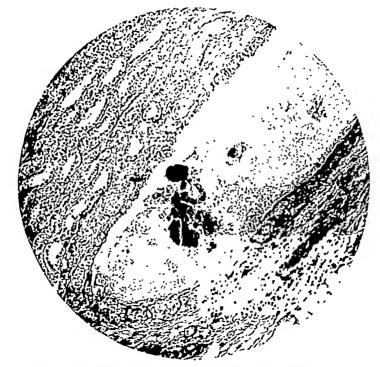
FIG. 310.—Oxamide stones in pelvis, showing also mucin deposit. (× 71.)

epithelium showed the granules.   This suggests that (when there is a pathological lesion present) there might be some change of function in the direction of concentrating.

In 3 cases in this series of 13 some diminution of tubular function had occurred in the ligated side, but it was not very marked.

f. No evidence of nerve degeneration has been demonstrated in the renal pedicle and no changes in the suprarenals noted.

Cases where Stones were Present (12).—Here an abnormality of the pelvic epithelium was the rule.   Marked desquamation was present in all cases, and frequently, if not always, the deposit of calcium in relation to these damaged

areas and around the desquamated epithelium was obvious. It seems clear from these appearances that stones are formed by deposition of calcium in relation to the injured epithelium (*Figs.* 308, 309).

Oxamide Feeding.—It was felt that it might be of interest to try other stone-producing diets in order to see if there were any predilection for the injured side —accordingly oxamide was used.

Ten rabbits were fed with oxamide, in addition to their normal diet, after preliminary ligature of a vessel in one kidney. In the kidney with a ligatured vessel five definite stones were formed (*Fig.* 310). They were quite large and hard.

In the normal kidney one formed definite stones, while in one other case one small concretion was present (presumably a stone). Occasionally fine granules of oxamide could be seen in the surface of the mucosa, but these occurred equally on both sides.

It appears from this series that oxamide stones also are more likely to form in the kidney the blood-supply of which has been reduced.

As a further variation of this experiment an attempt was made to slow up the blood-flow by partial obstruction of the renal vein. It was not found possible to do this without causing severe damage to the kidney, but in 1 out of 6 in this series the damage was less severe, and in this case a mass of large hard stones formed in the pelvis.

Fixation of the Kidney.—This was carried out in 5 animals by sewing the kidney capsule on to the last rib on the right side or to the posterior abdominal wall on the left side. At laparotomy, a month later, the kidney movements were markedly lessened and often imperceptible. No stones were formed in this series, neither was there any obvious difference in the calcium content of each kidney as determined by the histological method. It was concluded that there is no evidence that deficient movement in the kidney has any effect on its calcium metabolism.

The effect of urinary obstruction has also been investigated, and has been described in the previous paper.

SUMMARY AND CONCLUSIONS

The truth of Leriche and Policard's theory is demonstrated by this series of experiments. The two important factors in the production of stone seem to be :—

1. A dietetic factor, as, for instance, a calcium-phosphorus imbalance or excess of some foreign substance such as oxamide.

2. A local factor which leads to the precipitation of the stone-forming substances.

In view of the fact that the stones always form in the pelvis or calices it seems that a cavity is necessary. In all cases there was some abnormality of the epithelial lining, and frequently the stones could be demonstrated forming around desquamated epithelium. This suggests that an important factor in stone formation is an alteration in the epithelium which might act by producing variations in surface tension, or more directly by giving rise to desquamation, the dead epithelial cells then acting as a nucleus for the stone.

FIG. 311.—Keratinization in vitamın A deficiency. (× 140.)

FIG. 312.—Hyperplasıa of pelvıc epithelium and desquamation in vitamin A deficiency. (× 140)

This idea is confirmed by two other series of experiments which were carried out :—

1. A series of animals on a vitamin A deficiency diet was observed. It is not intended to describe these here except to say that in all cases where stones were formed, changes in the epithelium were marked, and indeed this is an effect well recognized. Calcium could be seen deposited around the desquamated epithelium, forming stones. *(Figs. 311, 312.)*
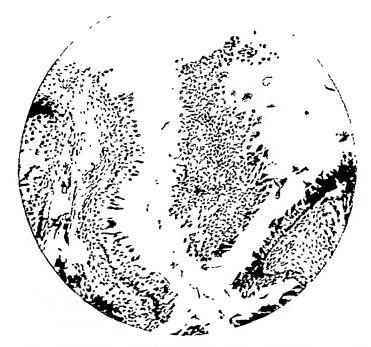
FIG. 313.—Desquamation of epithelium following salicylic acid injection. (／ 126.)

2. In this series and in another series of rabbits on this diet or being fed with oxamide no stones were found in the bladder. If, however, the vesical epithelium had been damaged previously by an injection of 0·5 c.c. of salicylic acid in 1–1000 alcohol solution, stones formed as follows *(Fig. 313)* :—

In a series of 26 fed on the lime and vitamin D diet—
13 preliminary salicylic acid injections—stones formed in 2.
13 no salicylic acid injections—stones formed in 0.

In a series of 10 fed on oxamide—
5 had preliminary salicylic acid injections—stones formed in 3.
5 had no preliminary salicylic acid injections—stones formed in 0.

Other factors which were noted were an alteration in the reaction and an increased production of mucoid material. It is quite possible that these might be of influence in the initiation of the process of stone formation.

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SHORT NOTES OF RARE OR OBSCURE CASES

BILOCULAR STOMACH DUE TO HERNIA OF THE SMALL BOWEL THROUGH THE TRANSVERSE MESOCOLON

By N. R. BARRETT

SURGICAL UNIT, ST. THOMAS'S HOSPITAL, LONDON

HERNIA of the intestine through the transverse mesocolon is rare, and in a recent paper Menegaux[1] was able to collect from the literature only 59 undoubted cases. It is, however, a condition with which surgeons should be familiar, for it is seldom diagnosed before operation and therefore presents itself unexpectedly; even when the abdomen is opened the true state of affairs may remain in doubt, a fact shown by two cases in which a laparotomy was undertaken and in which the hernia was discovered at the autopsy. When recognized, and except in cases of acute obstruction, the treatment is straighforward and the prognosis is good.

The first accounts were given by Loebl in 1844, Dittrich in 1847, Deville in 1851, and Treitz in 1857. All these dealt with post-mortem material, and it was not until 1902 that Akerman published the first description of an operation upon such a patient. His case had a gastric ulcer situated on the lesser curve of the stomach, and it was not till he started to do the posterior gastro-enterostomy that the hernia was discovered.

From time to time the recorded cases have been collected and analysed by various workers,[1-6] and the remarks at the end of this report are based upon the observations in these papers and upon the points which presented themselves in the present instance.

The interest of the present case lies in the fact that the hernia arose spontaneously and was unassociated with trauma or any previous operation, and that it has been successfully treated by surgery.

HISTORY.—The patient, a woman of 45, gave the following history. At the age of 16 she first began to suffer from intermittent attacks of colicky abdominal pain. The pain, which was sometimes severe, was felt in the lower part of the abdomen and round the umbilicus. After several years the attacks wore off and her general health improved.

Eight years later the pains returned and were aggravated by severe flatulence and vomiting; they were localized at this time to the epigastrium, but were unlike the pains associated with an ulcer in the stomach or the duodenum in that they bore no relation to food and were not relieved by drugs or diet. The vomiting became steadily worse over a period of months, and then, quite suddenly, all symptoms abated and the patient became normal except that she was prone to occasional attacks of flatulence.

She remained well for about twenty years, and then her troubles returned in the form of flatulence and diffuse abdominal pain. Both these symptoms increased in severity till she finally came to hospital to know if anything could be done for her. The attacks were now described as being most severe after a large meal; the symptoms would persist for about two hours and would gradually wear off, leaving a feeling of soreness in the epigastrium. She knew of no method of relieving the pain; she was never sick. There was no history of hæmatemesis or melæna.

ON EXAMINATION. — The patient's general condition was found to be good and there were no physical signs in the chest or the abdomen to account for her symptoms. As an out-patient a barium meal was arranged and the state of affairs shown in *Fig.* 314 was discovered. On this X-ray a diagnosis of bilocular stomach, due presumably to a lesser-curve ulcer, was made, although the history did not seem to fill the bill.

Two months later after a course of medical treatment a second X-ray was taken and the outline of the stomach was unchanged (*Fig.* 315). She was accordingly admitted for investigation.

A test-meal showed a normal quantity of hydrochloric acid both before and after histamine. The test for occult blood, which was returned as positive, was of doubtful value since she was found to be suffering from hæmorrhoids. Unfortunately a complete barium meal was never done.

FIG 314 —Before operation. X-ray of stomach taken directly after a barium meal. Report by Dr. Fildes: Grossly bilocular stomach without local tenderness. A spastic type of deformity presumably from a small ulcer not definitely seen

OPERATION.—A laparotomy was advised and at the operation the explanation of her troubles was discovered. On opening the peritoneal cavity part of the pancreas, the small intestine, and the edge of the spleen presented; the stomach and transverse colon were not seen at this stage. She had a mass of calcified mesenteric glands binding the great omentum down to the right side of the pelvic brim. After freeing the omentum a hole in the transverse mesocolon about the size of a five-shilling piece was discovered, and through this three-quarters of the small intestine had passed into the lesser sac. There was no hernial covering derived from the mesocolon.

The gastro-hepatic omentum was practically non-existent and the coils of the small bowel had passed forwards between the lesser curve of the stomach on the left and the portal vein, hepatic artery, and the bile-duct on the right. In this way the body of the stomach was pinched between the intestines passing up into the lesser sac posteriorly and out over the anterior surface of the stomach in front of the transverse colon. The hernia was easy to reduce, and there were no adhesions in the upper part of the abdomen.

The mesocolon was repaired, but it was not possible to draw the edges of the gastro-hepatic omentum together since the vessels in front of the foramen of Winslow were almost completely exposed for the greater part of their course.

The stomach was then examined and was found to be divided into two distinct parts by a narrow isthmus. The site of the isthmus corresponded to the place where the coils of the small bowel had encircled the viscus. There was no evidence of ulceration or fibrosis in the stomach wall, and although it is possible that the organ might have readjusted itself in time it was thought that a gastrogastrostomy was necessary to ensure a fairway. The pylorus was examined and although the X-rays suggested the presence of pyloric stenosis nothing abnormal was found and it was deemed unnecessary to do a pyloroplasty.

FIG. 315.—Before operation X-ray of stomach taken directly after a barium meal This photograph was taken two months after that shown in Fig. 314.

At the conclusion of the operation the greater curvature of the stomach, and with it the spleen, had fallen back into their normal positions.

There was nothing in the vicinity of the transverse mesocolon to suggest the cause of the defect, and it was assumed to be congenital in origin. The pains which the patient experienced as a girl may have been due to tabes mesenterica, and the binding of the great omentum to the pelvic region probably occurred at this time and limited the space normally available for the jejunum. As the patient grew older the jejunum passed into the lesser sac and round the stomach, causing attacks of subacute obstruction characterized by flatulence and vomiting.

She made a good recovery from the operation and the X-rays taken three weeks and seven weeks later show that although some degree of pyloric stenosis

remains the stomach is otherwise quite normal (*Figs.* 316, 317). She states that her pains have been completely relieved and that she is now fit and well.

DISCUSSION

It may be of interest to give a brief summary of the main points which are known about herniæ through the transverse mesocolon.

They occur more commonly in women than in men and manifest themselves between the ages of 25 and 50.

Diagnosis is always difficult and the number of cases in which it has been made correctly before operation is very small.

The cases can be divided into four main clinical groups. In the first are those whose lesion is discovered post mortem and who, during life, have had no symptoms of the disease; in the second are patients who complain of vague digestive disturbances; the third group are those who have evidence of small bowel obstruction, which may be either acute or chronic; and the fourth are diagnosed as suffering from a gastric or duodenal ulcer or an hourglass stomach.

The interpretation of X-rays, which alone can give the correct diagnosis before operation, is apt to be misleading, for on several occasions where a barium meal has been given an hour-glass stomach has been found. The clinician and the radiologist have been satisfied that this explained the symptoms, and consequently the passage of the medium through the small bowel was not investigated. On the other hand, a complete barium meal will demonstrate the loops of small bowel above the lesser curve of the stomach, and this is absolutely diagnostic.

FIG. 316.—X-ray taken three weeks after operation. Barium meal showing six hours' residue in stomach. Gastro-jejunostomy functioning well, but appearance of pyloric stenosis.

The treatment is laparotomy with reduction and repair of the hernial orifice, and it is here that a knowledge of the various types of hernia which have been described may save the surgeon a great deal of trouble in working out the lie of the land, for on opening the abdomen the small bowel usually presents, and it may be difficult to find the stomach and transverse colon.

There are two types of hernia.   The first has a sac formed from the thinned-out mesocolon.   This is a rare condition and the hernia is usually small.   The common variety has no sac and the two omental cavities communicate directly with each other.

It is usual for the small bowel to be drawn into the lesser sac, but cases are on record in which the stomach has passed downwards.   It seems that in the majority of cases the small intestine is sucked up by the excursions of the diaphragm,

and it is not uncommon for all the small intestine and even the cæcum to pass through the hole.   In two cases the hernia recurred at operation as soon as it had been reduced, and it was only with difficulty that the bowel could be maintained in its anatomical position.

Except in the early cases the bowel does not remain in the lesser sac but pushes onwards and either comes through the foramen of Winslow (this is very rare) or else perforates the gastro-colic or the gastro-hepatic omentum. The latter is the common course, and, in the words of Menegaux, the small intestine " se répand alors en cascade devant l'estomac et le côlon transverse", and in so doing it compresses the stomach so strongly at the point where the mesentery rounds the lesser curve that the stomach is divided into two parts.   In examining the recorded cases one finds that sometimes the

FIG 317 —X-ray taken seven weeks after operation   Stomach rather dilated and to the left of the mid-line   Empties slowly via a deformed cap   Some degree of pyloric stenosis remains

hour-glass deformity is due to spasm and sometimes it is associated with a simple or malignant ulcer.

Unless strangulation has occurred reduction is always easy, for there are no strong adhesions and the hole is large.   Practically the only cases in which adhesions have been described are those in which the transverse colon and the omentum have been involved as well as the small bowel.   The flimsy texture of the transverse mesocolon presumably accounts for the rareness of cases that have been strangulated.

There is usually no difficulty in repairing the transverse mesocolon, but in almost all cases the colic vessels have been described as lying in the margins of

the hole and the sutures must be placed in such a way that the blood-supply of the colon is not disturbed. When it has been impossible to repair the defect by simple means the posterior aspect of the stomach has been used to stop the gap. This was the plan adopted by Mayo in the case he recorded.

It is important to remember that in at least 50 per cent of the cases a gastric or duodenal ulcer has been found, and this lesion may need surgical treatment after the hernia has been repaired. Other abnormalities, such as volvulus of the stomach, have been described, but are not present sufficiently frequently to need emphasizing.

The pathology of the condition remains a matter for debate. In many cases there is a history of trauma followed by the signs and symptoms of an internal hernia ; in others a gastro-enterostomy has been done and the hernia has occurred because the mesocolon has not been closely sutured round the anastomosis. There are cases in which the only solution seems to be that the defect is congenital. Some authorities argue that the gastric ulcer is the important predisposing factor, but it is more likely that the ulcer is the result and not the cause of the hernia, for the peritoneum does not usually respond to inflammation by becoming fenestrated, the absence of adhesions is very definite, and the ulcer is usually quite a long way from the hernial orifice.

The number of cases which have been operated upon is small, but in the absence of acute obstruction the results of surgical treatment have been very satisfactory.

I am indebted to Mr. C. Max Page, Director of the Surgical Unit, under whose care this patient was admitted to St. Thomas's Hospital, for permission to treat and to publish this case, and to Dr. Fildes, who kindly provided the X-ray photographs.

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[6] REINHARDT, *Zeiglers Beitr. z. pathol. Anat.*, 1917, lxiii, 649.

A MALIGNANT TUMOUR (SYMPATHICOBLASTOMA) OF THE SUPERIOR CERVICAL GANGLION

By FRANK T. LAND

ASSISTANT SURGEON, GLASGOW EAR, NOSE AND THROAT HOSPITAL

SCOTT and Palmer (1932) have classified tumours arising in the sympathetic nervous system according to their degree of differentiation, thus following the scheme proposed by Bailey and Cushing (1926) for neoplasms of the central nervous system. The type most frequently encountered in the autonomic system is the ganglioneuroma, which is composed of mature ganglion cells and is usually a simple growth. In contrast with it at the other end of the scale is the highly

malignant sympathicoblastoma, a tumour formed by rapidly proliferating embryonic sympathetic cells. It occurs most frequently in infancy and early childhood, and usually originates in the suprarenal medulla. The sympathetic plexuses of the abdomen, thorax, or neck are only rarely the site of origin. The present case is an example of the last type.

HISTORY.—C. S., a boy aged 4 years, was brought to hospital in January, 1931, with the complaint of pain in the left ear of fourteen days' duration. It was not severe and was accompanied by slight otorrhœa. Soon after the onset the parents noticed a swelling below the left ear, and remarked on the impaired movement of that side of the face. Swallowing had occasionally been difficult, the attempt inducing spasms of coughing. Latterly the child's appetite had been poor and his sleep disturbed by earache. With the exception of slight rickets the previous health had been good, and there was no history of former ear trouble.

ON EXAMINATION.—The child was listless and inattentive : the temperature was sub-febrile. Facial paralysis of peripheral type was present on the left side. The pupils were markedly unequal, the left being contracted but reacting to light and in accommodation. The left anterior and posterior auricular glands were enlarged, while the jugulo-digastric group formed a mass about the size of a pigeon's egg below the tip of the mastoid process. The glands were fairly discrete and were not tender. There was no œdema over the mastoid, which was moderately tender at the posterior border and at the tip. The auditory meatus contained some pus, removal of which revealed what appeared to be granulation tissue obscuring the tympanic membrane. There was profound deafness on that side without loss in bone-conduction. Spontaneous vertigo and nystagmus were absent. The mouth and pharynx appeared to be normal, but the presence of pharyngeal anæsthesia could not be determined.

X-ray films of the mastoids showed loss of cellular definition and an irregular clear area below the antrum on the affected side.

At operation on the mastoid removal of a thin cortex revealed a uniformly whitish friable tissue, which almost entirely replaced the mastoid cells and extended into the auditory meatus, the digastric groove, and the posterior cranial fossa. As the appearance at this stage suggested an inoperable sarcoma radical operation was not attempted, but specimens were taken for histological examination. On receipt of Dr. Blacklock's report that the tumour was a highly malignant, undifferentiated sympathetic growth, deep X-ray therapy was instituted. One exposure of 600 r. over the region of the swelling resulted in considerable diminution in its size. A fortnight thereafter the tumour commenced to grow rapidly once more, and the child died with symptoms of meningitis six weeks later, i.e., ten weeks from the onset of the illness.

AUTOPSY.—Dr. Blacklock performed an autopsy and found a mass of tumour tissue in the neck, extending upwards from the region of the superior cervical ganglion. It was not encapsulated and had invaded the surrounding muscles. The internal carotid artery and the jugular vein were surrounded by the tumour tissue, which also enclosed the glossopharyngeal nerve, the pharyngeal branch of the vagus, and some cervical nerve-roots. Spreading upwards the growth had invaded the mastoid through the digastric groove. Where it had broken through the compact bone on the posterior surface of the petrous, small protuberances

were formed under the dura. At no place, however, had the latter been penetrated. The jugulo-digastric lymph-glands were enlarged, discrete, and whitish in colour. No other secondary growths were found, and both suprarenals were normal both on naked-eye and microscopic examination. Death had occurred apparently from basal meningitis, which was the only other lesion present.
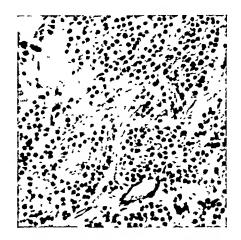
FIG. 318 —Section of tumour from region of superior cervical ganglion showing masses of small darkly-staining cells and fairly abundant fibrils. (*Hæmatoxylin and eosin.*) (× 200.)

Portions of the tumour tissue from the region of the superior cervical ganglion and from the mass in the temporal bone were examined microscopically. The growth was almost entirely composed of small round cells with deeply staining nuclei and scanty cytoplasm. Some larger cells with more abundant cytoplasm and vesicular nuclei were found, but no mature ganglion cells were discovered. After a careful search of a number of sections imperfect pseudo-rosettes were observed, but mitotic figures were scanty. Fibrillar material was present scattered irregularly throughout the tumour and was most plentiful in the specimens from the mastoid extension (*Fig.* 318). It stained yellowish in iron hæmatoxylin and van Gieson preparations, and greyish-black by the Cajal method. The cervical glands in the neighbourhood of the tumour were extensively invaded.

DISCUSSION

In a young child the clinical syndrome characterized by otorrhœa of painless onset, mastoid tenderness, glandular enlargement, and facial paralysis is almost invariably the result of tuberculous infection of the middle-ear and mastoid. In the present case, however, the additional features of myosis and dysphagia, attributable to involvement of the sympathetic, vagus, and glossopharyngeal nerves, suggested a more extensive lesion, probably of malignant nature. The histological appearances proved to be those of a sympathicoblastoma, only slightly differentiated. It seems reasonable to presume that it arose in the superior cervical ganglion. The position and direction of spread of the tumour, and the absence of any other nearby source of sympathetic cells, makes it tolerably certain that it originated in, rather than invaded, the ganglion. Burghard (1900) found that operative removal of the superior ganglion produced, in addition to myosis, unilateral flushing of the face and intense and persistent headache. Of these features myosis alone occurred in our case.

Excluding those arising in the medulla of the suprarenals, malignant tumours of the autonomic nervous system have been very infrequently recorded. In 1932 Scott and Palmer reported a case of intrathoracic sympathicoblastoma, and made an extensive survey of the literature. They found references to 31 cases, in the greater number of which the tumour affected the abdominal plexuses. Martius

(1913) recorded the post-mortem findings in the case of a child of 2½ years who was operated on for the relief of dyspnœa. The tumour, a sympathicoblastoma, originated in the middle cervical ganglion and compressed the trachea. The histological features of a similar rapidly growing neoplasm in an infant of 9 months have been described by Stewart (1919). Arising in the upper cervical region the growth bulged into the pharynx and was thought at first to be an abscess. Indeed, a quantity of pus was released by incision. Rapid growth continued and an attempt at removal was unsuccessful, the child surviving for only a few hours. An autopsy was not permitted. Von Fischer (1922) recorded a rather more differentiated tumour occurring in the neck of a still-born child. Capaldi (1927) described the case of an adult in whom neoplasms of the inferior cervical ganglion and the adrenal medulla invaded the vertebral canal causing paraplegia. Shirai (1933) has recorded an instance, also in an adult, of a tumour of the cervical sympathetic with metastases in the mucosa of the stomach.

When the cranial bones are invaded by sympathetic-cell tumours it is almost invariably in the form of metastases of a primary suprarenal growth (Blacklock, 1934). The orbit is then commonly affected and exophthalmos a striking feature (Greig, 1929). Tileston and Wolbach (1908) and Blacklock (1934) have recorded instances where the abdominal tumour was not apparent for some weeks after the appearance of cranial metastases. In the present case we assumed that there was probably a primary adrenal growth, and so we were discouraged from persisting with radiation therapy despite its temporarily favourable effect.

I have pleasure in thanking Dr. J. W. S. Blacklock for his reports on the histological and post-mortem examinations, and for the illustration.

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REVIEWS   AND   NOTICES   OF   BOOKS .

Clinical Pathology of the Jaws : with a Histologic and Roentgen Study of Practical Cases. By Kurt H. Thoma, D.M.D., Charles A. Brackett Professor of Oral Pathology in Harvard University, etc. Large 8vo. Pp. 643 + xii, with 423 illustrations. 1934. London : Baillière, Tindall & Cox. 38s. net.

In the Preface the author writes, " In many respects the jaws have been the ' no man's land ' of the human body. They are of no particular concern to the average physician, because treatment almost always involves a dental problem and he has no desire to interfere with the highly specialized field of the dentist ; conversely, the dentist primarily treats the teeth and has little experience in generalized diseases affecting the maxilla and the mandible." Surgeons and dentists will agree with this statement and will welcome this compendious volume as a serious and painstaking attempt to present an up-to-date account of what is known of the pathology and clinical aspects of diseases of the jaws.

Not only does the author include malformations, fractures, infections, cysts, and neoplasms of the jaws, but he has sections devoted to those changes induced by endocrine disturbances, nutritional disturbances, and general diseases of uncertain etiology, so that the volume contains a very complete account of this subject.

In our opinion the best part of this work is that which treats very fully of the various cysts that occur here ; in this, as in the other sections of the book, the author not only mentions cases that he has seen personally, but has also ransacked the literature of the subject and has searched the medical museums for specimens to illustrate his thesis. The numerous illustrations are excellent ; the coloured microphotographs, of which we should like to have seen more, are beautifully reproduced ; the X-ray reprints, as so often happens, are rather a mixed lot, and some of them are not very helpful to the reader.

There is an excellent bibliography, though with what to us appears to be an astonishing exception ; it is obvious that the author is intensely interested in the pathology of bone with its puzzling sequelæ of increase and decrease of calcification, yet he does not seem to be acquainted with the recent work of Leriche and Watson Jones ; at any rate, we can find no reference to it. We make the modest suggestion that, when a second edition of this work is called for, this omission should be rectified.

We believe this work will become the standard book of reference on the pathology of the jaws and we cordially commend it to the attention of surgeons and dentists.

The Story of the Middlesex Hospital Medical School. By H. Campbell Thomson, M.D. (Lond.), F.R.C.P., Consulting Physician to the Department for Nervous Diseases, the Middlesex Hospital, etc. Large 8vo. Pp. 182 + xiii. Illustrated. 1935. London : John Murray. 10s. 6d. net.

The story of the Middlesex Hospital Medical School is told well and pleasantly by Dr. H. Campbell Thomson, Consulting Physician to the Charity and a former Dean of the School. It is written on the occasion of the hundredth anniversary of the foundation of the Medical School.

The Hospital began in a small way in the middle of the eighteenth century and soon became a centre for students working at the Hunterian School. The clinical teaching, at first quite informal, became systematized when Sir Charles Bell, who had bought the Windmill Street School, was elected Surgeon to the Hospital. Students from his school followed him to the Hospital, and so long as he remained in London they attended in considerable numbers. When he left, the Middlesex Hospital staff established a proprietary school on the lines then usual. It languished for some years, but was reorganized and made to flourish by a strong medical and surgical staff aided by a succession of self-sacrificing deans. The school was united with the Hospital in 1896, and from that time to the present has gone forward steadily to become, as it now is, one of the great teaching centres in London.

Dr. Campbell Thomson tells of all the changes, modestly omitting mention of the share he himself took in them. He gives an account of the great physicians and surgeons who were on the staff, pointing out that Dr. William Hunter was never officially attached to the Hospital, though he once acted as locum tenens for the man-midwife. There is, too, an account of the life led by medical students in the middle of the last century, showing that Dick Swiveller was hardly a caricature and might as easily have been a student at the Middlesex as at Guy's. There are many good illustrations.

King's and Some King's Men. Being a Record of the Medical Department of King's College, London, from 1830 to 1909, and of King's College Hospital Medical School from 1909 to 1934. By H. WILLOUGHBY LYLE, M.D., F.R.C.S., Fellow of King's College, London; Dean Emeritus of King's College Hospital Medical School, etc. Royal 8vo. Pp. 613 + x. Illustrated. 1935. London: Humphrey Milford. 25s. net.

THIS volume, which Mr. Willoughby Lyle has entitled *King's and Some King's Men*, has an especial interest for surgeons. It is a history of the medical department of King's College, London, from its foundation in 1830 to 1909. During that period J. Moncrieff Arnott, Joseph Henry Green, Sir John Simon, Richard Partridge, Sir William Fergusson, Henry Smith, John Wood, Lord Lister, and Watson-Cheyne had been members of the surgical staff. Sir William Bowman, beginning life as a physiologist and general surgeon, set the tradition of cultured ophthalmic surgery which has been so successfully followed by Mr. Willoughby Lyle himself. It is not surprising that with such masters the Hospital formed a true nursing mother for its surgical pupils. Well trained, they went to all parts and did much good work in advancing surgery. Pridgin Teale at Leeds, C. P. Childe at Portsmouth, Johnson Smith at Greenwich, Nottidge Macnamara at Calcutta, McDougall, Bishop of Labuan and Sarawak, in the Far East, Christopher Heath, John Whitaker Hulke, Edward Bellamy, Thomas Bond, Thomas Nunn, George Lawson, and Sir John Tomes in London. Sir William Bowman's teaching was reflected in Richardson Cross of Bristol, in Edward Nettleship, George Critchett, and Gustavus Hartridge. All were great men in their different spheres, and all are given their due meed of praise by Mr. Willoughby Lyle.

The book is a mine of information and is well worth reading as the story of the progress of an institution from very small beginnings to its present position in the world of English medicine. The book is well illustrated and there is an excellent index.

Surgical Diseases of the Chest. By EVARTS AMBROSE GRAHAM, A.B., M.D., F.A.C.S., Professor of Surgery, Washington University School of Medicine, St. Louis; JACOB JESSE SINGER, M.D., F.A.C.P., Associate Professor of Clinical Medicine, Washington University School of Medicine, St Louis; and HARRY C. BALLON, M.D., C.M., F.A.C.S., formerly Assistant Professor of Surgery, Washington University School of Medicine, St. Louis. Large 8vo. Pp. 1070, with 637 illustrations. 1935. London: Henry Kimpton. 65s. net.

THE publication of a book on thoracic surgery by such authorities as Graham and his co-workers will inevitably interest those who have attempted to follow the rapid advances in this increasingly important branch of surgery. These authors indicate that an appeal to the physician seems even now to be particularly desirable, as there is still an insufficient appreciation on the part of medical men in general of the help in many conditions which a surgical attack offers. A perusal of the table of contents would certainly lead one to believe that there are few chest diseases, either of themselves or in their complications, in which surgical measures have not been attempted. The nature of their undertaking is best illustrated by the extensive bibliography appended at the end of each chapter, subdivided into corresponding sections to the text. This bibliography amounts in total to almost one hundred pages, and as the great majority of references refer to papers published in recent years, accounts for the difficulty of keeping up to date a book which necessarily takes several years to complete. In spite of these obvious difficulties, or perhaps because of them, the authors are the more to be congratulated.

The first chapter, on physiological considerations of importance to the thoracic surgeon, largely embodies the previously published views of Graham which are now widely accepted, and this section merits careful consideration from all surgeons who are called upon to treat patients with any intrathoracic condition.

The short section upon anæsthesia is frankly disappointing and well below the general standard of the book. A wide discussion upon more recent forms of anæsthesia and the question of premedication was to be expected.

The surgery of the heart, pericardium, and large vessels occupies nearly eighty pages, and a full account is given of every condition amenable to surgical methods. The recent work on angina pectoris by sympathectomy, alcohol injection of the sympathetic, and by thyroidectomy receives consideration.

Pulmonary suppuration apart from bronchiectasis, carcinoma of the bronchi, the œsophagus, and diaphragm, each have chapters devoted to their special pathological conditions. A separate chapter by David H. Ballon on diseases of the trachea and bronchi endoscopically considered, although well written and illustrated, has resulted in a somewhat unnecessary overlapping and repetition of conditions previously or subsequently considered.

The last portion of the book is devoted to the treatment of pulmonary tuberculosis by artificial pneumothorax, oleothorax, cauterization of adhesions, and the recognized purely surgical measures of phrenicectomy, plombage, and thoracoplastic procedures. The latter in view of their great importance would appear to be much less fully discussed than cardiovascular conditions, in which surgical measures are much less frequently attempted or required.

Unquestionably the best section in the book is that devoted to bronchiectasis. This condition is considered from every aspect—etiology, pathology, diagnosis, prognosis, and treatment all being considered in detail. In view of changes during the last two years, an unduly pessimistic view of the radical treatment by lobectomy is indicated. This impression is somewhat diminished, however, by perusal of the preface to the book.

Descriptions of illustrative cases throughout add considerably to the value of the text, and the inclusion of a large number of illustrations, diagrammatic drawings, and radiograms is to be commended. To those without experience in thoracic surgery a measure of dogmatism is often advisable in such a text-book, but this may well be a fault in a subject where changes are so rapid.

There can be no doubt that this book fulfils an essential need at the present time, will repay reading, not only by surgeons but by physicians, and as a book of reference is invaluable.

BOOK   NOTICES

[*The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest for our readers*]

La Maladie des Pêcheurs d'Eponges nus. By SKEVOS ZERVOS   Large 8vo.   Pp. 29. Illustrated.   1935.   Paris : Libraire J.-B. Baillière et Fils.   No price given.

Estudos cirurgicos (First Series). By ENRICO BRANCO RIBEIRO (Santa Catharina).   Large 8vo.   Pp. 241.   Illustrated.   1934   Sao Paulo, Brasil : Sociedade Editora Medica Limitada.   No price given.

Diseases of the Liver, Gall Bladder, Ducts and Pancreas : their Diagnosis and Treatment. By SAMUEL WEISS, M.D., F.A.C.P., Clinical Professor of Gastroenterology, New York Polyclinic Medical School and Hospital, etc.   With a chapter by J. P. GRANT, M D , F.A.C S , M.R.C S., and A. J. QUIMBY, M.D., F A C R.   Imperial 8vo.   Pp 1099 + xxviii, with 358 illustrations and 6 coloured plates   1935.   New York : Paul B Hoeber Inc. $10 00.

A Guide to the Surgical Paper : With Questions and Answers. By R. J. McNEILL LOVE, M.S. (Lond.), F.R.C S., Surgeon, Royal Northern and Metropolitan Hospitals, etc.   F'cap 8vo.   Pp. 78.   1935.   London : H. K. Lewis & Co. Ltd.   5s net.

The Theory and Practice of Anæsthesia. By M. D. NOSWORTHY, M.A., M D., B Ch. (Cantab.), Anæsthetist to Westminster Hospital, etc., with a Foreword by I. W. MAGILL, M.B., B.Ch (Belfast), Anæsthetist to Westminster Hospital, etc.   Crown 8vo   Pp. 223, with 35 illustrations.   1935.   London : Hutchinson Scientific.   12s. 6d. net.

IPSISSIMA VERBA

BY SIR D'ARCY POWER, K.B.E., LONDON

VIII. HUTCHINSON'S TRIAD : THE TEETH

JONATHAN HUTCHINSON, born in 1828, died 1913, came of a Quaker family in Yorkshire. He settled in London after an apprenticeship in York, became attached to the Moorfields Eye Hospital in 1862, was Surgeon to the London Hospital until 1883, and was President of the Royal College of Surgeons of England in 1889. Observant and full of ideas, he soon realized that syphilis was being treated to relieve symptoms not to cure the disease. The actual cause was unknown, but as early as 1876 he stated that it was due to a specific and living microbe, contagious and transmissible only so long as it retained its vitality. " Some one will see it one day for it is beyond doubt that it must be there." That day he lived to see, for on March 3, 1905, Fritz Schaudinn showed Erich Hoffmann that spirillum which was called afterwards *Spirochœte pallidum*.

Hutchinson was insistent that syphilis needed prolonged treatment and was a pioneer in the administration of small doses of grey powder for many months, but never to salivation. His treatment, therefore, was in direct opposition to the method of the majority of his contemporaries, who gave large doses of corrosive sublimate only so long as the symptoms or signs of the disease were present.

As Surgeon to the Eye Hospital he was early interested in interstitial keratitis, which was not then uncommon, and he observed that many of these patients also had malformed teeth.

The first-fruits of his observations appeared in the paper contributed to the Pathological Society, May 10, 1858 (*Trans. Pathol. Soc.*, 1857-8, ix, pp. 449-456). It was referred to a Committee to report, the Committee consisting of Dr. Graily Hewitt, Mr. Henry Lee, and (Sir) Henry Thompson, who sent in a guarded report dated July 14, 1858. Hutchinson says :—

" For a considerable time past I have been in the habit of recognizing in a certain very peculiar development of the permanent teeth an indication that their possessor had in infancy suffered from hereditary syphilis. A remark to this effect, which I made at a meeting of the Pathological Society early in the past session being received with expressions of incredulity, it occurred to me, that it might be well to make public such evidence as I possessed on the subject. With that view, the facts which are the basis of the following report were

collected.   My friend, Mr. Coleman, our dentist at the Metropolitan Free Hospital entered with zeal into the subject, and readily agreed to take casts of the teeth of any patients I should send him.

"Most of the cases taken, were those of patients attending at the Royal Ophthalmic Hospital on account of chronic interstitial keratitis, an affection which is, I believe, almost always a result of inherited syphilis.   Their ages varied from twenty-eight years to five years.   In all a clear history of syphilis was established, either by the free confession of the patient's parents, or by the account given of

FIG. 319.—Hutchinson's teeth   (*From Power and Murphy's ' A System of Syphilis ',*
and by kind permission of Dr. G. F. Still)

symptoms of undoubted character during infancy.   The number of casts taken was thirteen and in all instances a stereographic portrait of the patient was also secured, which in many instances, illustrates very well the peculiar physiognomy impressed by the disease.   With these remarks as to the nature of the evidence I will now pass to the conclusions arrived at.

"*That there is a peculiar condition of the teeth, which results from the influence of hereditary syphilis and that the most frequent features of this condition are the following :—*

" *a. Smallness.*—The teeth stand apart with interspaces, and are rounded and peggy in form, instead of flat.

" *b. Notching.*—They usually exhibit in their border a broad shallow notch, or at times, two or three (serrated). Owing to their softness ; these teeth rapidly wear away, and this notching is thus often obliterated, but when markedly present, it is one of the most decisive conditions.

" *d. Colour.*—Instead of the clear smooth, white exterior of good teeth, they present a dirty greyish surface, totally destitute of polish and rarely smooth. No amount of cleaning will materially alter this feature which owes its existence, I believe, to the great deficiency of enamel.

" *e. Wearing down.*—As before observed their softness from deficiency of enamel renders them liable to premature wearing down. The teeth of a syphilitic patient not twenty will often be ground down as much as those of a very old person should be, and this in cases in which there is no peculiarity as to position, such as the front teeth meeting in the bite. An unusual degree of wearing down if coexistent with other peculiarities is then a suspicious condition. .

" *f.* The signs mentioned apply almost exclusively to the incisors and canines, and in fact the grinders are usually altered in a very much less degree. Their surfaces are often more uneven than those of healthy teeth, and now and then they present tubercular projections of very peculiar character.

" These conditions are totally distinct from those produced by the ravages of caries. Very often the mouth of an hereditarily-syphilitic patient will present a full set of teeth quite free from decay, but all of them marked with features of unmistakable peculiarity. As a general rule, however, they are very liable to caries. Of course it is only when several of the conditions enumerated exist together, that a confident opinion can be given, and then it is the regularity of the type, and the fact that it marks all the front teeth in both jaws, which offers the best means of distinguishing it from other forms of disease or irregularity.

" The above remarks apply only, to the permanent set. The milk-teeth of syphilitic-infants, are liable to exfoliate before being cut, and after having been cut, are often of small size, bad colour, and very liable to decay, but the notching and the peg-like form are rarely noticed."

SPONDYLITIS ANKYLOPOIETICA

(*Spondylitis Ossificans Ligamentosa*)

By F. CAMPBELL GOLDING

RADIOLOGIST, ROYAL NATIONAL ORTHOPÆDIC HOSPITAL, LONDON

THE condition considered in this report is that affection of the spine associated with the names of von Bechterew, Strümpell, and Pierre Marie. It has been shown by Buckley[5] and Llewellyn[24] that this condition was described most ably by an English physician, Dr. Bernard Connor, in 1700, more than one hundred years before the work of the continental authors to whom credit is given.

At the present time the word ' spondylitis ' (qualified by the type of organism which is considered responsible) is used as a generic term for lesions of the spine. In the case of ankylosing spondylitis, it has become the custom in some quarters to differentiate types of the disease according to the situation to which symptoms are referred at the outset of the disease, associating with these types the names of one of the above authorities. Thus in the Bechterew type the upper dorsal spine, and in the Marie-Strümpell type the lumbar spine is the first site where rigidity appears, and in spondylitis rhizomélique (Marie and Leri[17]) the large proximal joints are also involved. In this investigation it appeared that the Marie-Strümpell and rhizomélique spondylitis were the same disease, the sub-division being justified no doubt for descriptive purposes.

It has been difficult to interpret what is understood by the Bechterew type from the literature on the subject. Bechterew[4] described a fixed dorsal kyphosis with meningeal involvement and degenerative changes in the cord, associated with symptoms of paresis and altered sensation in the appropriate segmental region. Marie and Astie[16] showed in addition the influence of trauma and heredity in these patients. Few of the patients who are described in the recent literature conform with this description, and in this investigation a clear type which could be classed as ' Bechterew's disease ' was not recognized.

It is not denied that spondylitis ankylopoietica (Zigler[23]) affects the dorsal and cervical regions ; in fact the early clinical evidence is often a dorsal kyphosis, which is more or less fixed, but from the radiological examination there is rarely evidence of the cause of this kyphosis, or alternatively when calcification of ligaments is present in this region, it will usually be found to be present in a more marked degree in the lower thoracic and lumbar spine.

ETIOLOGY

In common with many of the conditions classed as rheumatic disease, the etiological factors of spondylitis are uncertain. It is customary to refer to toxæmia (Marie and Leri[17]) and the influence of temperature and trauma (Kaufmann[14]). Other observers have considered the disease an example of a metabolic disorder,

and recently the parathyroid glands have been incriminated and have been removed in some patients (Hoffmeister,[11] Oppel,[18] and Ballin and Morse[2]). Others have stated that the disease is a form of rheumatoid arthritis which attacks the spine (Jones,[13] Knaggs[15]). The theory which has found most favour is that the disease is of infective origin, but direct evidence to support this in all cases is difficult to obtain.

No writer has produced evidence that spondylitis is more common in the manual than the sedentary worker : 93 per cent of patients in this series lived within fifteen miles of London and 73 per cent led sedentary lives ; 23 per cent were manual or outdoor workers such as policemen, gardeners, etc. Only 4 patients suggested in their history that they had been subjected to any particular strain or exposure to which the condition might have been attributed.

Radiographs were secured of 124 patients, 106 males and 18 females. Of these, 79 males and 12 females presented the clinical and radiographic features of spondylitis ankylopoietica. The remainder, 27 males and 6 females, had sacro-iliac joint disease without changes in the spine ; in spite of this, 6 bore a clinical diagnosis of spondylitis ankylopoietica.

Holbrook[12] and others have remarked on the high percentage of males affected by this disease. Of their 22 patients, all were males and all were protected types, e.g., dentists, accountants, etc. In 1912 Dardel[6] stated that only two instances had been described in females, one by Gasne and one by Aldaroff.

Of this series, the age was known in 114 individuals. These were divided into two groups : Group I, with a clinical or radiographic diagnosis of spondylitis ; and Group II, with changes in the sacro-iliac joints alone. The average age of Group I, when presenting for treatment, was 36 years, and the average age when symptoms began was 25 years. The average age of Group II at the corresponding times was 28 years and 23 years respectively ; there is a fairly close resemblance between the last two figures in each of these groups.

Six individuals were excluded from Group I. These were patients with advanced calcification of spinal ligaments ; in each instance the patient gave a history of less than six months' duration. It was obvious that this could not be true, as it was doubtful if the changes which were visible could have been produced in as many years, and on these grounds they were excluded.

The high incidence of this disease in the young adult male militates against a metabolic origin, since at this time metabolic disturbances are notoriously rare.

Based on the work of Oppel,[18] of Leningrad, parathyroidectomy has been performed by surgeons in Germany and America. Oppel says : " The results of this operation may be considered very encouraging, for it primarily destroys the hypercalcæmia, thereby stopping the process of progressive ankylosis, and this is indeed the most important principle to be affected by the operation." Quoted by Oppel is Belsgorodsky, who found that all his patients suffering from ankylosing polyarthritis had an increase in the calcium content of the blood. In Oppel's own patients, 28 out of 42 had a raised blood calcium value, while 14 had a normal level.

Hoffmeister[11] describes the result of parathyroidectomy on a patient with advanced spinal rigidity, the cervical spine alone being stiff but not fixed. The blood calcium was reduced by two operations from 18 mgrm. to 14 mgrm. to 10 mgrm. per cent, and the blood phosphorus from 3·4 to 3 mgrm. per cent.

Ballin and Morse[2] state that " Multiple ankylosing arthritis should also be included in the chapter on parathyroidism. The metastatic calcification around infected joints, especially vertebral joints, is based on a moderate hypercalæmia."

The blood of a number of these patients was examined by Dr. Shackle at the British Red Cross Clinic for Rheumatism. The figures for the blood calcium were :—

1. 12·9 mgrm. per cent. No spinal changes. Sacro-iliac joint involved
2. 12·1   „   „   „   No spinal changes. Sacro-iliac joint involved
3. 12·6   „   „   „   No spinal changes. Sacro-iliac joint involved
4. 11·0   „   „   „   Early calcification of ligaments. Sacro-iliac joint involved
5. 11·4   „   „   „   Moderate calcification of ligaments. Sacro-iliac joint involved
6. 12·1   „   „   „   Moderate calcification of ligaments. Sacro-iliac joint involved
7. 12·6   „   „   „   Moderate calcification of ligaments. Sacro-iliac joint involved
8. 9·5   „   „   „   Advanced calcification of ligaments. Sacro-iliac joint involved
                                   (No evidence of activity)

In so far as these figures are of any significance, they confirm a slight hypercalcæmia in some patients, especially in the earlier types. In a few instances the inorganic phosphorus was estimated in addition :—

1. 11·6 mgrm. per cent (Ca). 3·76 mgrm. per cent (P)
      Advanced calcification of ligaments, sacro-iliac joint involved

2. 11·8 mgrm. per cent (Ca). 3·35 mgrm. per cent (P)
      Advanced calcification of ligaments, sacro-iliac joint involved

3. 10·1 mgrm. per cent (Ca). 5·8 mgrm. per cent (P)
      No spinal changes, sacro-iliac joint involved

There have been many patients in this collection whose history and clinical examination revealed a focus to which the disease might have been reasonably attributed, either in the form of gonorrhœa, ulcerative colitis, or septic tooth or antrum. But there was a lack of uniformity in these findings. Many individuals appeared quite free of infective foci.

Of these conditions, gonorrhœa and its sequelæ have been given great prominence (Whitman,[22] Jones and Lovett[13]). In this series only 9 patients gave a definite history of gonorrhœa. It is not suggested that this in any way represents the true number who had been affected by this disease. The investigation was not carried out with this point in mind, largely because of the difficulty in proving or disproving a past infection many years after the subsidence of the disease. In this connection it may be mentioned that iritis of a type which tended to recur (one patient had had four attacks) was present in 5·6 per cent of instances. There appeared to be some relationship between this and a past gonorrhœal infection, but the number was too small to draw any useful conclusions. The gonococcal complement-fixation test was carried out in a number of instances. A positive result was a rare event and the case was not included unless corroborated by the history.

The blood sedimentation rate was examined in a number of individuals. These were divided into two groups : Group I, with sacro-iliac joint changes and ligamentous calcifications ; Group II, with sacro-iliac joint changes alone. It can be seen that in Group I the values are more consistently raised and that Group II shows peculiar variations. Some of these patients were examined more than once over a period of two years, and in these circumstances the average value is given :—

GROUP I			GROUP II		
1.	58 mm.		1.	110 mm.	
2.	100 mm.		2.	123 mm.	
1.	9 mm.		1.	6·5 mm.	
2.	26 mm.		2.	14 mm.	
1.	63 mm.	Average of 2	1.	23 mm.	Average of 3
2.	92 mm.	examinations	2.	50 mm.	examinations
1.	38 mm.	Average of 2	1.	5 mm.	
2.	68 mm.	examinations	2.	13 mm.	
1.	40 mm.		1.	75 mm.	Average of 7
2.	75 mm.		2.	110 mm.	examinations
1.	78 mm.		1.	57 mm.	
2.	110 mm.		2.	90 mm.	
1.	25 mm.				
2.	52 mm.				
1.	22 mm.				
2.	41 mm.				
1.	26·4 mm.				
2.	49 mm.				
1.	31 mm.				
2.	60 mm.				

There is a certain similarity in the radiographic appearances of rheumatoid arthritis and spondylitis, especially when the smaller joints are involved, but it does not appear that this is sufficient at present to justify the assumption of their common origin.

The calcification of ligaments extending some distance from the joints, as seen in the spine, the rib articulations, and hip-joints, is not a feature of rheumatoid arthritis. The age and sex incidence of the two are also dissimilar and there is no explanation of the fact that the spine is involved so seldom in rheumatoid arthritis and the minor joints so infrequently in spondylitis.

PATHOLOGY

Marie and Leri[17] considered that spondylitis rhizomélique began as a rarefaction of vertebral bodies which then produced a reactive hyperossification of ligaments. Simmonds[20] believed the most important feature was the ossification of ligaments surrounding joints and extending some distance from these joints. Ehrhardt[7] postulated a syndesmogenous synostosis of all vertebral joints with ossification of ligaments.

The German workers, amongst whom are Siven,[21] Fraenkel,[9] Rumpel,[19] Beadle,[3] and Schmorl, believe the process begins in the capsule and articular surfaces of the intervertebral facets in the form of an ulcerating disease. Several patients have been examined at autopsy. Siven[21] in 1903 reported four instances, of which one was examined at autopsy. He found the most advanced changes in the joints between the ribs and the spine, where there was total ankylosis, and the intervertebral discs were only slightly diseased. He concluded that it was an inflammatory disease of the joints which led to complete ossification of the spine.

Güntz[10] in 1933 summarized the present view of this school. From the post-mortem examination of an early case and correlation with nine patients with advanced disease in Schmorl's collection of spines, he concluded that the disease consists of an inflammation of the small joints of the spine, with round-cell infiltration, hyperæmia, and, above all, connective-tissue formation. The final result is ossification of articular surfaces. All stages of the disease are found in different joints.

Some joints may escape. No changes are found in the bodies of the vertebræ in early stages, and the changes which take place in these structures and in the ligaments during the course of the disease are of a secondary nature. Unfortunately the radiographs of this patient were not published; it would have been an advantage to see the stage of the disease as described.

The information gained from a post-mortem examination is greater than can be obtained from any number of radiographs, but there is no record of the post-mortem condition of the sacro-iliac joints in these patients. This important point has been overlooked. Yet radiographs reveal that in every instance these joints are involved.

FIG. 320.—An example of sacro-iliac joint disease. There is irregular destruction of the joint margins, with some sclerosis of subarticular bone. Note the intervertebral joints, most of which show clearly and do not appear to be involved. There is an absence of calcification of ligaments.

FIG. 321.—A rare type with very marked sclerosis of bone associated with a long history. No calcification of ligaments.

From the study of the radiographs I am of the opinion that the changes in the sacro-iliac joints precede destruction of the cartilage of the intervertebral facets and precede calcification of ligaments. It can be contended that the facets are involved before or at the same time as the sacro-iliac joints, but owing to the limitations of radiographic technique this involvement cannot be shown. It is true that the radiograph will only show gross pathological changes in the facets, but there were many cases in the series in which there was well-marked sacro-iliac disease with apparently normal intervertebral joints, and others with a longer history in which both the sacro-iliac and intervertebral joints are obviously involved. As described by Güntz, normal and diseased intervertebral joints were seen in the presence of

calcification of ligaments, especially in the early stages of calcification. In this series it was noted that these normal facets were the more rare, the more advanced the calcification of intervertebral ligaments. In the last stage, i.e., the bamboo spine, no normal facets were found. (*Figs.* 320–337.)

THE SACRO-ILIAC JOINT

It has been shown that the sacro-iliac joint is not a synchrondrosis since it possesses the essentials of a true joint (Albee[1]). It is affected as a secondary process in many diseases, of which tuberculosis is probably the most common. It is also subject to many congenital and age variations, and the lower edge of the ilium is frequently grooved by large blood-vessels entering the pelvis, producing an appearance of lipping of this edge, simulating osteo-arthritis. The radiographic interpretation of these joints is extremely difficult and all the aids of radiographic technique are necessary to produce good results.

FIG 322 —Nov 10, 1932   FIG 323 —Feb 26, 1935.

FIGS 322, 323 —Showing progressive calcification of ligaments of the spine associated with sacro-iliac joint disease Note that the only intervertebral facet which can be seen appears irregular. The others are probably obscured by ankylosis

One or more authors in France, Germany, America, and England have remarked on the fact that the sacro-iliac joints tend to be involved in a certain percentage of instances of spondylitis ankylopoietica. When examining these radiographs it was

FIG 324 — Feb 19, 1930

FIG 325 — Feb 19, 1930

FIG 326 — Sept 24, 1931

FIG 327 — July 30, 1935
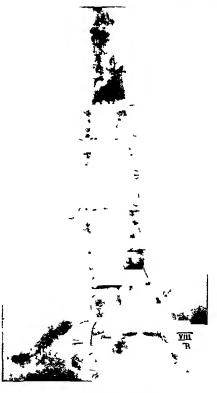
found that the sacro-iliac joints were involved in all instances in which there was the typical calcification of ligaments of spondylitis, and it was noticed that this was the case in even the earliest examples—that is, those with only a few strands of calcification between vertebral bodies. A few individuals were found also with what appeared to be the same process in the sacro-iliac joints, but no calcification of ligaments. Several of these were found to have rigidity of the spine on clinical examination, and others complained of generalized pains without symptoms in the back. In every instance the radiographic appearances indicated the same disease process in the sacro-iliac joints, early in some, more advanced in others.
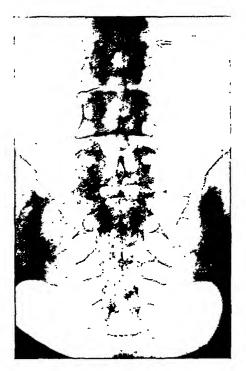
FIG. 328.—July 30, 1935.

FIGS. 324–328.—The sacro-iliac joint disease can be seen in the radiograph taken of the hip on Feb. 19, 1930. At this time the whole spine was radiographed and is clear. Unfortunately no further films were made of the sacro-iliac joints at this time. On Sept. 24, 1931, there is still no calcification of ligaments apart from a doubtful lesion between Thoracic XII and Lumbar I; the changes in both sacro-iliac joints can be seen. In the last film, early calcification of ligaments can be seen at the site which was previously clear. The sacro-iliac joints are now ankylosed.

The changes in these articulations consist of an irregular destructive process affecting the joint surfaces, and the clear definition of the anterior and posterior edges of the joints, as seen on a radiograph, become blurred and serrated. Next the cartilage space is destroyed and slight sclerosis becomes evident in the periarticular bone of the sacrum and ilium. The amount of destruction and sclerosis varies considerably in different individuals, but both proceed until the joint is destroyed, when ankylosis takes place; the sclerosis then becomes less marked and eventually there is continuity of bone between the sacrum and ilium with little or no trace of the joint.

FIG. 329.—Oct. 27, 1927.
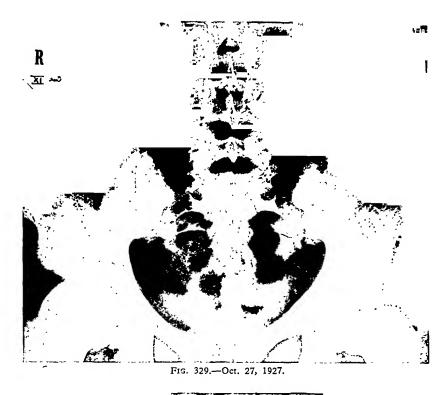
FIG. 330.—Oct. 12, 1934.

At present the stage of ankylosis represents the customary state of affairs when the changes of spondylitis ankylopoietica are manifest and the diagnosis of this disease is made.

It has been mentioned that the destructive changes which precede ankylosis, before there is calcification of ligaments, are also believed to be manifestations of
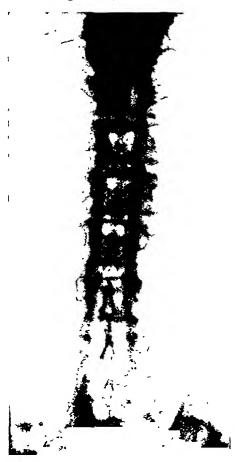
FIG. 331.—Oct. 12, 1934.

FIGS. 329–331.—In the first film (Oct. 27, 1927) both sacro-iliac joints are involved, showing a broad irregular joint space due to destruction of the joint margins. In the second film there is complete ankylosis of both these joints and the hip-joints. There is also advanced calcification of the lumbar ligaments. The last film (also Oct. 12, 1934) is included as it shows the so called 'tram-track' type of calcification of ligaments. Fortunately the patient had kept his earlier radiographs and it is possible therefore to show the earliest type of change in the sacro-iliac joints and the fully advanced disease. There is an interval of seven years between these examinations (Figs. 329, 330).

spondylitis or, more correctly, to be evidence of a prespondylitic condition. Most orthopædic surgeons and practitioners in physical medicine are familiar with patients in whom spinal rigidity is taken to indicate the presence of spondylitis ankylopoietica but in whom the radiographic examination reveals no visible changes in the spine.

Sir Robert Jones[13] has said in reference to the X-ray diagnosis of spondylitis : " In the absence of positive signs, the diagnosis must be made by exclusion and often a period of observation will be necessary before reaching a final conclusion." In other words, in its early development spondylitis passes through a period when the clinical history and physical signs are in favour of the diagnosis but this cannot be confirmed by radiology. It is suggested that radiographs should be taken of the sacro-iliac joints at this time.

THE CHANGES IN LIGAMENTS

This feature, consisting in the deposition of calcium in ligaments, thereby rendering them opaque to X rays, has been described by many writers. These changes may be seen in the anterior and posterior longitudinal ligaments and the

FIG. 332.—An example of the moderately advanced disease. The sacro-iliac joints are seen in the early stage of ankylosis with a trace of activity still present. Note that only the remains of the intervertebral joints can be seen.

ligamenta flava, producing a streaky appearance of the bones, especially in the lower lumbar region, often made more obvious by the associated decalcification of the bodies. Or there may be a ' tram-track ' effect when the ligaments of the interarticular facets are calcified—namely, two opaque parallel lines on either side of the mid-line, or a single line in the median plane if the interspinous and supraspinous ligaments are affected. The ' bamboo spine ' is produced by calcification of the ligaments round the intervertebral discs. These varieties are shown in *Figs.* 331 and 333. Other ligaments may show changes—for example, the radiate

ligaments of the heads of the ribs, the pubo-capsular and ilio-femoral ligaments in the hip, and ligaments of the pubic symphysis.

A survey was made of the radiographs to determine the most common site for the earliest changes in the spine. This was found to be between the vertebræ on either side of Thoracic XII and between Lumbar IV and Lumbar V. There were, of course, many exceptions to this statement, but this appeared to be the region of predilection, in spite of the prominent symptom of rigid dorsal kyphosis.

Other points noted were: the intervertebral discs were of normal width in spite of advanced changes in the ligaments around them; the decalcification of the bodies was often marked but was not necessarily an early sign; the streaky type of calcification was most obvious in the lumbar spine between Lumbar II and Lumbar V.

A peculiar manifestation of the disease was seen in some of the bones; it was difficult to decide whether this was a superficial osteitis without condensation or was due to changes in the ligaments at their insertion into bone. It was found, as a rare event, in advanced histories in the ischial tuberosity, the patella, and os calcis; seen apart from the spinal condition it would be most difficult to interpret correctly.

THE PRE-SPONDYLITIC HISTORY
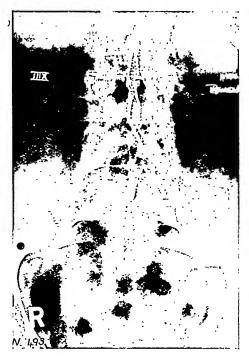
A comparison was made of the early history of patients with fully developed spondylitis with those in whom sacro-iliac disease only was present. The march of symptoms which occurred early in the disease, described by those who had advanced changes in the spine when they came to examination, was strikingly similar to that in patients who had sacro-iliac disease only, and this suggested that there is a definite type of clinical history associated with this disease in the early stages. In this connection the age and sex of the patient is of considerable importance.

The pre-spondylitic history consisted of a number of attacks of pain of a fibrositic character recurring over several years, with free intervals. These pains were referred to the muscles or the neighbourhood of joints and were associated occasionally with a synovitis, which tended to resolve without deformity, especially in the peripheral joints. The site of muscular pains appeared to be most commonly in the thighs and buttocks, and varied from vague pain noticed especially on commencing movement after a period of rest, to severe attacks sufficient to incapacitate the individual. It was fairly characteristic that these pains, in any limb, tended to be in the proximal rather than the distal segments. The trunk was also affected, the complaint being made of 'tightness round the chest', etc. Many patients stated that these symptoms were worst when they were tired, or when in bed at night, interfering with sleep, and that they were relieved by exercise after a preliminary difficulty in commencing movements. A small number of patients gave a history of an acute onset with swelling of many joints, resembling rheumatic fever, but differing in that pain tended to persist after the swellings subsided. In such individuals ultimate limitation of movement was uncommon in these joints. The diagnosis of the true condition would appear to be impossible in this acute phase. Apart from this type, there were cases with a slow onset of swelling in one joint.

Distal joint involvement is believed to be a rare event in spondylitis ankylopoietica, and it was seldom present at the time of examination, but relying on the patient's statement, one or more joints had been swollen, presumably owing to

FIG. 333.
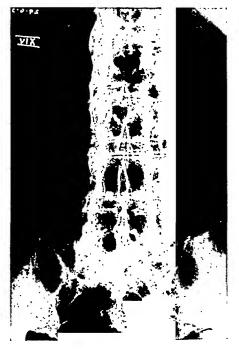
FIG. 334.

FIG. 335.

FIGS. 333–335.—The three types of end-result as seen in the lumbar spine: *Fig.* 333, The bamboo spine; *Fig.* 334, The 'streaky' type; *Fig.* 335, A combination of these two. The sacro-iliac joints are ankylosed. No intervertebral joints are visible.

synovitis, in 23 per cent of instances. The knee-joints were involved most frequently, the sternoclavicular joints in only two cases.

Restricted movement was rare in the distal, but common in the proximal, joints; it tended to be bilateral, and was present in 13·7 per cent in the shoulder and in 12·9 per cent in the hip; often both were affected in the same individual.

There were two exceptional instances in which the hip-joints were attacked early, with a severe onset, accompanied by great pain. These patients lay in bed afraid to move, with the joints slightly flexed; although there were early spinal changes these were overshadowed by the condition in the hips, and the diagnosis was not made until radiographs were taken.

FIG 336.   FIG 337.

FIGS 336, 337.—Fig 336 is an example of the predominant calcification of the interspinous ligaments, simulating an Albee graft   Fig 337 shows the changes, as described, which occasionally occur in the ischial tuberosity and elsewhere in bone   This is the same case as shown in Fig 334

Sciatica was fairly common as an early symptom, but it did not appear to differ from the ordinary interstitial neuritis. Of the whole series, 11·2 per cent had been diagnosed by doctors as sciatica at some time, 14·5 per cent as fibrositis or muscular rheumatism, and 7·2 per cent as infective arthritis. It is possible that these diagnoses were correct and that the early symptoms of spondylitis were due to inflammatory changes in fibrous and connective tissue.

After a varying period of pain in the limbs with or without remissions, the complaint began to be made of stiffness and pain in the back. This became more or less constant, and from this time onwards the diagnosis became more easy with each succeeding year.

In taking the histories of these people, one became so accustomed to the type of complaint which has been described under the ' pre-spondylitic period,' that it was difficult to believe the patient who stated that symptoms began in the back and not in the muscles and joints.   Without any doubt this does occur, but it appeared to be more rare than the first type of onset.

So constant were these symptoms that it was believed to be a justifiable procedure to radiograph the sacro-iliac joints in any case of fibrositis in a young adult male who gave a history of recurring attacks which had not responded to treatment or had responded temporarily.   After the age of 30 years the possibility of this examination proving of any value is more remote.

DIFFERENTIAL DIAGNOSIS

There are relatively few conditions which can be confused with spondylitis ankylopoietica.   Spondylitis muscularis and senilis (Knaggs[15]) are variations of the same condition, due to muscular weakness with secondary dorsal kyphosis ; there is some narrowing of the discs on the anterior border, calcification of ligaments is absent, and the vertebral bodies may be much decalcified.   The late stage of kyphosis adolescentium does not present difficulty, since there is no calcification of ligaments, and the wedged irregular vertebral bodies in the later stages are typical of the condition.

The most important differentiation is from osteo-arthritis of the spine.   There are several articles in the literature in which no distinction is drawn between these two conditions.   In most instances of osteo-arthritis the patients are over fifty years of age or there is a history of strain, the so-called ' labourer's spine '.   A paper has been written recently by Forestier and Robert[8] on the differentiation of osteophytes and calcification of ligaments.

If radiographs are taken, the diagnosis should not present great difficulty ; usually most of the stages of these conditions can be seen on the single film, and the early formation of an osteophyte is unlike the calcification of ligaments.   The osteophyte is frequently a thick, blunted, bony process projecting at an angle from the margin of the vertebra.   The early calcification of a ligament is a thin-pointed homogeneous deposit running from one body to another in the form of an arc of a circle.

PROGNOSIS

The more or less hopeless prognosis of fully developed spondylitis is well known.   The situation is more grave than in the average instance of rheumatism, since the sufferer is nearly always a young adult male who, after a varying period, is not able to earn a living.   It appears that the condition does not progress invariably to the complete ' bamboo ' spine ; some patients reach a stage of limited mobility, with subsidence of subjective symptoms.

It is difficult or impossible to form an opinion on the prognosis in early stages from the symptoms and radiographs of the spine.   It has been noted all through this series that the most severe instances were those with the greatest destruction of the sacro-iliac joints, and that those with mild changes in these joints, often difficult to detect, had infrequent attacks of pain, insufficient to produce incapacity.   It was observed also that the fully developed ' bamboo ' spine was always associated with

destruction of the sacro-iliac joints, with bony ankylosis so complete that the previous position of the joint could be determined with difficulty.

In contrast to this the condition in which there occurred calcification of a few ligaments only, which did not alter materially in two or three years, was usually associated with what was believed to be a mild process in the sacro-iliac joints, often accompanied by sclerosis of the subarticular bone.

The patients who answered the follow-up letters by saying they did not need to attend as they were cured or were progressing satisfactorily without treatment were all individuals who had what was interpreted as a mild or quiescent disease of the sacro-iliac joints. It is suggested as a reasonable conclusion that some idea of the prognosis can be gained from a scrutiny of the sacro-iliac joints.

TREATMENT

This subject is only considered from the general aspect of the course of the disease as shown by clinical and X-ray examination. It was evident that it will always be difficult to assess the value of any form of treatment in this disease.

Firstly, the normal advance of the condition is so slow that a period of years may be necessary to observe additional calcification of ligaments. It is necessary, therefore, to rely on clinical findings, such as the relief of pain, freedom of movement, gain in weight, etc. This is complicated by the fact that patients without treatment may have periods of relief and exacerbation. Some of these patients terminated treatment, as they felt they were cured or had obtained such relief that treatment did not appear to be necessary, only to return months or years later with a fresh attack. This applied more particularly to patients with only sacro-iliac joint disease.

Secondly, the disease sometimes appears to wear out, a stage being reached in which, although there is a fixed kyphosis, muscular pains occur infrequently and there is some recovery of general health. In this case the particular treatment which the patient is having at this time will receive credit which may not be justified.

CONCLUSIONS

The radiographs of 91 patients suffering from spondylitis ankylopoietica have been collected, together with the history and clinical findings. In many instances additional examinations have been made with further radiographs.

It is believed that the diagnosis of spondylitis ankylopoietica may be made earlier than at present.

From a detailed examination of the early history of these patients it was found that almost all gave a long history of muscular and joint pains before the onset of spinal rigidity. This type of history was so constant that it was thought to be possible to recognize it at the clinical examination.

It was also found that in spondylitis of this type pathological changes in the sacro-iliac joints were invariably present. There were no exceptions to this statement in 91 patients.

In addition, 33 individuals had pathological changes in the sacro-iliac joint without spinal changes. These patients gave a history of the same type as the above, and 6 had been diagnosed, in fact, as spondylitis ankylopoietica by the clinician before radiographic examination.

From the information which has been gained from this collection of patients it is believed that sacro-iliac joint disease of this type is the earliest manifestation of spondylitis and may be present as a useful diagnostic indication for several years before the back is involved.

In addition, the etiological factors have been considered, with the blood sedimentation rate and blood calcium in some of the patients.

It is thought that some indication of the severity and prognosis of the disease may be obtained by the degree of activity of the process in the sacro-iliac joints.

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AN IMPROVED TECHNIQUE FOR THE INTRODUCTION OF RADIUM NEEDLES IN THE TREATMENT OF CARCINOMA OF THE BREAST

BY R. BROOKE

SURGEON, ROYAL WEST SUSSEX HOSPITAL

ONE of the greatest difficulties in the treatment of carcinoma of the breast by radium needles is to be sure that the needles when introduced lie parallel to each other. When the patient is prone—the position in which radium needles are usually introduced into the breast—the nipple is central or approximately central in position ; but when the patient sits up, as she does in bed after the operation, if the breast is at all pendulous the nipple comes to lie at a much lower level. It follows from this that radium needles lying parallel to one another when introduced are no longer parallel when the patient is back in bed. The shorter the needles, the more likely is there to be this alteration in their relationship. The breast is radiated unequally ; in one place there will be overlap, in another deficient radiation. In order to overcome this difficulty the following technique has been adopted :—

The various glandular regions, the axilla, supraclavicular fossa, infraclavicular region, intercostal spaces, and epigastric region are needled in the usual way. The technique adopted here is that usually described. It is performed at the same time as the breast is dealt with, but before the breast is needled. It is in the actual needling of the breast itself that the improvements have been introduced. Careful co-operation by the nursing staff is essential for the method to be described. The nurses and house men rapidly become interested and learn to carry out their part of the technique—a very important one—with the greatest skill.

On the day before the operation, when the patient is in bed, and before the breast has been prepared for operation, the sister of the ward or the house surgeon first carefully marks the outline of the breast on the skin with a skin pencil, including the tail of the breast extending up into the axilla. The area so marked out is carefully measured, and a piece of red paper is then cut out its exact size. This is pinned to the notes and bed-letter and is sent to the operating-theatre before the operation begins.

The breast is needled by means of long hollow trocars measuring $9\frac{1}{2}$ in. in length, with an outside diameter of $\frac{1}{16}$ in. and an inside diameter of $\frac{1}{12}$ in. Each has a lance point at the one end which is detachable, and is covered with a protective cap. At the other end is a flange and split pin with which the trocar is held and introduced, also detachable (*Fig.* 338). These hollow trocars will contain the radium needles. The ends are made detachable in order to facilitate the loading and unloading. They are introduced through metal channels situated 1 cm. apart on a square metal frame, the size of which is adjustable by means of bolts and screws at the four corners, and can be made to take the largest breast (*Fig.* 339).

Actually the instrument consists of two of these frames attached to one another 1 cm. apart, and with the grooves for the trocars running in two directions at right angles to each other. Thus when the trocars have been all introduced, there are two rows of them, each trocar lying 1 cm. apart from and parallel with its neighbour, and each row lying 1 cm. apart and at right angles to the other first row. A number of metal stops of assorted lengths, the largest being 3 cm. and
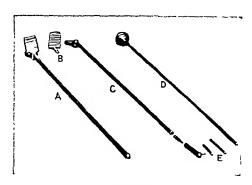
FIG. 338.—A, Trocar complete; B, Detachable flange; C, Trocar, showing detachable spear-point and cap; D, Stilette; E, Metal stops.

graduated in centimetres, and a stilette also graduated in centimetres and the length of the trocars, complete the apparatus (*see Fig.* 338).

The theatre sister receives the red paper outline of the breast, and placing it in the centre of the metal frame first adjusts the size of the metal frame until there is ⅓ cm. between the edges of the breast outline and the sides of the frame. She then takes the hollow trocars and inserts them through the grooves in the frame
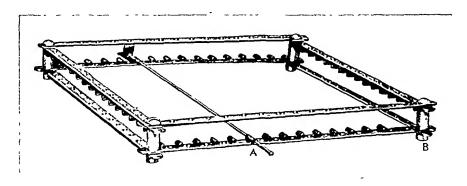
FIG. 339.—The frame. A, Trocar in position; B, Bolts for adjusting size of frame.

until the whole of the breast area has been covered. This manœuvre is repeated with the second row of trocars. The hollow trocars are now filled. Metal stops are introduced by means of the graduated stilette until the edge of the breast as indicated by the margin of the red paper is reached. Then radium needles are introduced throughout the length of the red disc, and when the other margin is reached, more stops until the trocar has been completely filled. The same process is repeated with the other trocars until in each row the portion of the containing
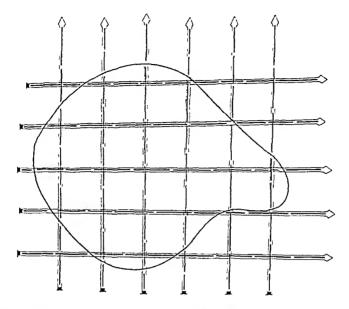
FIG. 340.—The parts of the trocars overlying the red paper are filled with radium needles, the other parts with metal stops.
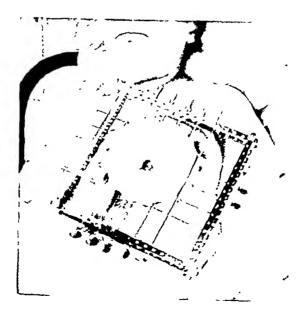
FIG 341.—The frame applied to the breast, showing how parallelism of the needles is assured.

radium needles exactly corresponds to the portion overlying the red paper (*Fig.* 340).

The frame is then marked top, bottom, right, and left sides, and with the trocars *in situ* sterilized. When sterilized the trocars are removed from the frame, greased with sterile paraffin, and laid in order on a sterile cloth ready for use by the surgeon.

Under a general anæsthetic, the frame is placed over the breast, and, taking care that the nipple is in the centre of the frame, the breast is pulled forwards and the middle of the base of the breast transfixed by the correct trocar. The trocars to the right and left are then introduced until the row is complete. The same procedure is then adopted with the second row of trocars, which are introduced at right angles to the first (*Fig.* 341). The caps are placed over the pointed ends of each trocar after they have been inserted. Light dressings are applied and the patient returns to bed. The trocars containing the needles are left in for a week, and at the end of that time are removed quite painlessly without an anæsthetic.

The advantage of this method of needling over other methods is that parallelism of the needles is assured. Actually when the breast is pulled forwards, the area of the base diminishes so that the area radiated extends for a short distance beyond the breast margin. This is an advantage. There are no gaps in the radiation, and the whole of the base of the breast is uniformly radiated. Secondary radiation is not an important factor.

The whole operation takes only ten to fifteen minutes, as against thirty-five to forty minutes when each radium needle is introduced separately and each thread anchored to the skin by a stitch. The time-taking part of the operation—namely, the loading of the containers—is all done by the sister or house surgeon before the operation begins. The needles are safely boxed up in a container, and the risk of loss is reduced to a minimum.

When the demand for radium exceeds the supply, it is not always possible to obtain the long radium needles which are essential if a breast is to be needled in the usual way. With this apparatus needles of any length can be used. The apparatus is tolerated extremely well by the patient, and the discomfort is negligible.

FURTHER OBSERVATIONS ON THE DISTURBANCE OF METABOLISM CAUSED BY INJURY, WITH PARTICULAR REFERENCE TO THE DIETARY REQUIREMENTS OF FRACTURE CASES

By DAVID P. CUTHBERTSON

GRIEVE LECTURER IN PHYSIOLOGICAL CHEMISTRY, GLASGOW UNIVERSITY

THE present writer has drawn attention to the marked loss of body nitrogen, sulphur, and phosphorus which occurs in the urine of otherwise healthy individuals who are in receipt of moderate or serious traumatic injury (Cuthbertson, 1930, 1931, 1932, 1934). This loss was observed to begin within a day or two following the injury, to reach a maximum within ten days, and then slowly to decline. It was noted that there generally occurred parallel increments in the basal consumption of oxygen, body temperature, and pulse-rate. It was suggested that this loss was probably more general than local, as in one fracture case 137 grm. N, equivalent to about 4·38 kilo. of muscle, were lost in the course of ten days. These phenomena were noted to occur in varying degree in uncomplicated fractures of the long bones, dislocations, effusions into joints, lacerations of soft tissues, and surgical incisions into knee-joints. In general the more severe the injury, the greater the catabolism. Other experiments indicated that the wasting of muscle and bone caused by immobilization, which of necessity occurs during treatment of fracture and knee-joint cases, was insufficient to account for the whole of this loss of substance, though it was undoubtedly a contributing factor. Although there was in most cases an evident initial depression of metabolism following the injury, the counter swing which followed was in excess of an immediate restitution.

As the accompanying fever was generally slight or scarcely appreciable in the milder cases, and as a study of pneumonia cases both before and after the crisis had failed to reveal catabolic effects in excess of those noted in severe injuries to the limbs, in particular those due to direct violence, it was considered that the loss of body substance was not proportional to the fever.

It was believed that these changes were the result of the organism catabolizing its reserves to meet the exigencies of repair and maintenance rather than due to the sweeping out of the disintegration products of the damaged tissues. The question naturally arose whether increased intake of foodstuffs could stem this loss of body substance or at least lessen its disintegration. The present communication is an attempt to determine this point: in addition certain other phenomena associated with injury are described.

EXPERIMENTAL

The patients were supplied with the requisite foodstuffs prepared in an appetizing form. It was generally found that after about a fortnight of high protein diet their appetite failed, and though the patients were still willing to co-operate they could not ingest the required amount.

Table I.—Summary of Results of Experiments in Eighteen Cases of Fracture

CASE	AGE	PERIOD OF OBSERVATION RECKONED FROM DAY OF ACCIDENT	NATURE OF INJURY	TOTAL CALORIES	N INTAKE (GRM.)			MAXIMUM URINARY EXCRETION OF N (GRM.)	DAY OF MAXIMUM URINARY N EXCRETION RECKONED FROM THE TIME OF ACCIDENT	N EXCRETION (GRM.) EXCLUDING FIRST THREE DAYS OF OBSERVATION			N BALANCE EXCLUDING FIRST THREE DAYS OF OBSERVATION (No. of Days)
					Basal N	Additional N and Source	Total N for Period (Average Daily)			Urine	Faeces (Average Daily)	Total N for Period	
1	43	2–14	Fractured humerus	1981	128·40	—	128·40 (14·27)	21·87	10th	154·90	11·52 (1·28)	166·42	− 38·02 (9)
2	59	3–14	Fractured humerus	1944	127·40	—	127·40 (14·16)	15·89	9th	135·01	8·64 (0·96)	143·65	− 16·25 (9)
3	24	2–17	Fractured tibia	1802	172·21	45·23 (Bovril)	217·44 (16·84)	36·18	7th	375·34	21·58 (1·66)	396·92	− 179·48 (13)
4	35	2–13	Fractured tibia and fibula and laceration of foot of one leg	914	34·92	85·05 (Lemco)	119·97 (13·33)	21·98	7th	171·92	8·28 (0·92)	180·20	− 60·23 (9)
5	23	1–15	Fractured tibia and fibula of one leg	1183	136·60	1·404 (Cystine)	138·00 (11·50)	29·10	9th	286·42	3·36 (0·28)	289·78	− 151·78 (12)
6	17	2–14	Lacerated tendo Achillis	2200	153·80	14·91 (Glycine)	168·71 (16·87)	19·31	6th	171·61	11·80 (1·18)	183·41	− 14·70 (10)
7	37	1–12	Fractured tibia and fibula of one leg	1669	109·80	25·20 (Glycine)	135·00 (15·00)	28·85	6th	219·78	6·45 (0·72)	226·23	− 91·23 (9)
8	21	2–22	Almost complete fracture of both bones of one leg	1990	196·20	47·88 (Eatan)	244·08 (13·56)	21·56	11th	338·65	17·46 (0·97)	356·11	− 112·03 (18)
9	20	2–14	Fractured tibia	3259	119·50	199·74 (Gelatin)	318·24 (31·82)	42·36	5th	370·36	12·48 (1·25)	382·84	− 64·60 (10)

No.	Age	Period	Injury										
10	25	2–16	Fractured tibia and fibula of one leg	3097	117·84	347·40 (Gelatin)	465·24 (38·77)	43·31	7th	464·10	13·08 (1·09)	477·18	— 11·94 (12)
11	23	2–27	Fractured humerus with bruising and laceration over supra-orbital ridge	2386	217·92	531·36 (Sodium caseinate)	749·28 (32·57)	38·51	6th	726·53	36·50 (1·59)	763·03	— 13·75 (23)
		5–14		2386	99·88	243·54 (Sodium caseinate)	343·42			365·38	17·63	383·01	— 39·59 (10)
		15–27		2386	118·04	287·82 (Sodium caseinate)	405·86			361·15	18·87	380·02	+ 25·84 (13)
12	26	2–12	Compound fracture of tibia and fibula of one leg	5392	79·55	227·70 (Sodium caseinate)	307·25 (34·14)	42·39	11th	342·29	15·84 (1·76)	358·13	— 50·88 (9)
13	42	2–11	Fractured tibia and fibula at lower end of one leg	3557	166·74	—	166·74 (23·82)	30·69	6th	197·62	5·91 (0·84)	203·53	— 36·79 (7)
14	35	2–17	Compound fracture of tibia and fibula of one leg	3193	345·41	—	345·41 (26·57)	31·59	7th	354·99	17·68 (1·36)	372·67	— 27·26 (13)
15	38	3–15	Fractured tibia and fibula of both legs	3214	318·40	—	318·40 (31·84)	40·25	8th	318·89	17·10 (1·71)	335·99	— 17·59 (10)
16	23	1–18	Fractured tibia and fibula of one leg	3044	507·60	—	507·60 (33·84)	42·00	6th	523·72	29·70	553·42	— 45·82 (15)
17	44	2–21	Fractured tibia and fibula of one leg	3606	623·73	—	623·73 (36·69)	40·82	8th	609·78	39·44	649·22	— 25·49 (17)
18	31	2–13	Fractured fibula	4135	147·51	—	147·51 (16·39)	22·96	6th	172·05	11·36	183·41	— 35·90 (9)
19	16	1–8	Fractured tibia and fibula of one leg	3592	41·55	—	41·55 (8·31)	20·67	4th	80·12	9·00	89·12	— 47·57 (5)

Difficulty was experienced in deciding the period of time over which the net gain or loss of body substance should be assessed.   It was eventually decided to omit the first three days of diet from the final computation.   The experiments are arranged in groups, and, although not strictly chronological, this order is the more convenient.   The analytical methods used were in general similar to those adopted in previous experiments.

Urinary K was determined by the method of Kramer and Tisdall (1921) with slight modification.   After separation of the potassium cobalti-nitrite it was oxidized with a known excess of standard permanganate as in the original method, but the excess after oxidation was determined by the addition of KI (Kahlbaum) and titration of the liberated I_2 with N200 sodium thiosulphate.

Sodium in the urine was determined by the method of Kramer and Gittleman (1924) following the incineration of 50 ml. urine acidified with H_2SO_4 at as low a temperature as possible.   The residue was dissolved in water and made up to 50 c.c. :   1 ml. was then taken for analysis.

Preliminary experiments (*Cases* 1–12) were designed to determine if procedures such as daily massage (*Cases* 1, 2), the ingestion of meat extractives (*Cases* 3, 4), additional amounts of cystine or glycine (*Cases* 5–7), hydrolysate of mixed ox tissue (*Case* 8), or the addition of large quantities of proteins such as gelatin (*Cases* 9, 10) or sodium caseinate (*Cases* 11, 12) could stem the loss of body N when superimposed on diets of low first-class protein content and generally low caloric value.   It will be obvious from the later experiments (*Cases* 13–19) that no success could have resulted from these experiments, since the addition of large quantities of first-class protein to diets of high caloric content failed to maintain N equilibrium at the height of the catabolism.

Cases 1–8 were given diets of low caloric value in order to determine if the special agent which was being applied had an appreciable effect.

The Effect of Gentle Massage and Movements in the Treatment of Two Ambulant Cases with Fractured Humeri (*Cases* 1, 2).—*Cases* 1 and 2 were placed on diets of average first-class protein content (11·68 grm. and 14·16 grm. N per day respectively).   In the course of nine days *Case* 1 lost 38·0 grm. N and *Case* 2 lost 16·2 grm. N.   A kick from a horse fractured the humerus of *Case* 1 at the junction of the lower and middle thirds.   *Case* 2 was injured at practically the same site by a fall of stone.   There was also some bruising and laceration at the site of injury in the latter case.   The daily fluctuations in the urinary volume bore a fairly close relationship to the total N excretion.

In these two cases disuse atrophy was reduced to a minimum by allowing the patients freedom to walk about hospital and by massaging and manipulating the injured area daily from the date of injury.   It is evident that this procedure did not eliminate the loss of body N.   These two cases were the oldest of the series, being 43 and 59 years respectively.   This disparity may have been a factor in deciding the degree of catabolism.

The Effect of Meat Extractives (*Cases* 3, 4).—*Case* 3, who was on a moderately low first-class protein diet, received in addition 60 grm. meat extractive (Bovril) daily, equivalent to an extra 3·48 grm. N.   *Case* 4, who was on a very low first-class protein diet, received daily 100 grm. meat extractive (Lemco), equivalent to 9·45 grm. N.

In the course of thirteen days *Case* 3 (fractured tibia at junction of middle

and lower thirds) lost 179·4 grm. N (equivalent to about a stone of muscle if that be the source of this N), and in nine days *Case* 4 (fractured tibia at mid point with extensive laceration of one leg, skin having to be removed off part of distal half) lost 60·23 grm. N. On the thirteenth day following the accident *Case* 3 had an infarction of the lung and there was an abrupt rise of body temperature coupled with a slight rise in the urinary volume and N excretion. These rises subsided after three days, but the temperature subsequently rose and clinical evidence of pneumonic consolidation was present. Unfortunately this development concluded the biochemical record. It was apparent that even with definite fever the rise in N excretion was not as great as occurred in consequence of the initial injury.

Throughout the period of observation this case was on a constant intake of water, the volume of urine varying with the N excretion.

In *Case* 4 the basal oxygen consumption and body temperature curves fluctuated in parallel but not with the N excretion. On the eighth and ninth days following the injury there were abrupt rises in both the former curves although the N excretion was decreasing at the time. Subsequently there was a slight rise in N excretion, but this took place some four days later and may not have been related to the former events. A rise in body temperature and basal oxygen consumption is not necessarily accompanied by a rise in N excretion.

The Effect of Supplementing Diets of Average First-class Protein with Certain Amino Acids (*Cases* 5–7).—On the supposition that in these cases of injury the organism might require to catabolize its reserves to supply some essential amino acid in greater amount than was normally supplied in the diet— a condition analogous perhaps to the catabolism of body proteins in birds following the moulting period—1 grm. *l*-cystine was added daily to the low protein (mainly first-class) diet of *Case* 5. As the result of a fracture of both bones of the leg at the mid point this man lost 151·78 grm. N in twelve days. The urinary volume varied with the urinary N. Although the oxygen consumption rose with the rising urinary N output, it fell during the fourth to sixth days at a time when the N output continued to remain high. The rise in body temperature preceded that of N output and oxygen intake. The maximum temperature, 38·22° C., occurred on the second day.

To determine if there were any changes in the excretion of Na and K, the period of fifteen days was divided into three lots of four days each and one group of three days, and the average daily excretion of these elements determined for the various periods. K rose from 2·30 to 4·83 grm. per day during the third period— corresponding to the maximum N excretion—descending during the fourth period to 4·39 grm. Na, on the other hand, fell slightly during the second period, rising to the initial value by the fourth period.

The level of K in the blood serum fell slightly during this period. On the second, fifth, and eighteenth days its values were 23·1, 22·9, and 21·4 mgrm. per 100 ml. respectively. On these occasions the serum Na levels were 314, 348, and 294 mgrm. per 100 ml. These blood serum values are fairly constant: such variations as may appear significant are opposite in kind to those occurring in the urine. The corresponding blood urea N values were 23, 17, and 16 mgrm. per 100 ml., those of serum S 2·4, 0·9, and 0·8 mgrm. per 100 ml., indicating a definite initial rise in the level of these blood constituents, a rise which soon declined to normal.

As it has recently been suggested that glycine may play a part in the restoration to normal of the partially atrophied muscle fibres in cases of muscular dystrophy (literature reviewed by Cuthbertson and Maclachlan, 1934) it was thought of interest to feed glycine to one or two cases of traumatic injury.

Case 6, whose tendo Achillis had been severed by a reaping machine, received 10 grm. glycine daily throughout most of the period of observation in addition to a diet of average first-class protein content. In the course of ten days 14·70 mgrm. N were lost. The urinary volume varied with its N content but tended to rise still further. Body temperature also varied to some extent with urinary N.

Case 7, who had been knocked down by a motor-car with consequent fracture of both bones of one leg and considerable bruising, lost 91·23 grm. N in the space of nine days despite the addition of 15 grm. glycine daily to a diet of average first-class protein content. The tibia was fractured at the junction of the proximal and second quarters; the fibula at its head.

The urinary volume, urinary N, and body temperature tended to vary in parallel as occurred in the previous case.

As the process of testing out each amino acid in turn appeared to be wasteful without some positive indication, it was resolved to test out some palatable hydrolysate of mixed animal tissues.

Effect of Addition of a Hydrolysate of Mixed Ox Tissue (*Case* 8).—A palatable hydrolysate of mixed ox tissues was found in the preparation Eatan. About 71 per cent of the total N of this proprietary product is reported to be combined in amino acid form. To the rather low first-class protein diet of *Case* 8 were added daily 50 ml. (2·53 grm. N) of this mixture. The patient—a footballer with both bones of one leg fractured at the junction of the upper and middle thirds as the result of kicking an opponent's boot—lost 112·03 grm. N in the course of eighteen days. The urinary volume fluctuated with its content of N. During the gradual rise in N output there were periodic rises in body temperature, but these had passed off and the temperature had become normal before the maximum daily output of N was reached.

Since movement, certain meat extractives, and amino acids had all failed to stem the loss of body N in these injured men, it was thought that some measure of evidence might be achieved by adding certain incomplete proteins in large amount to the diets of injured persons.

Effect of Addition of Gelatin (up to 200 grm. daily) to Diets of Low First-class Protein Content (*Cases* 9, 10).—*Case* 9 fractured his right tibia at the mid-point as the result of indirect violence, there being no apparent displacement of the bone-ends. From the third to seventh days he received daily 120 grm. gelatin and then 150 grm. daily for six days. The basal diet was low in protein (mainly second-class) and normal as regards carbohydrate and fat. The patient lost 64·60 grm. N in ten days. Urinary N and volume ran parallel. When the gelatin was finally omitted from the dietary the urinary volume did not decline proportionally. The body temperature changes paralleled the N excretion. Preformed creatinine initially varied with the urinary volume and urinary N excretion, but later did not fluctuate with these changes, tending to remain fairly constant. The creatinuria was almost as great as the excretion of preformed creatinine. Increment in gelatin intake led to an increase in creatine excretion and decrease in intake led to a diminution in the creatinuria. This point will be discussed later.

Case 10, whose injury consisted of the fracture of both bones of one leg, at the mid-point, the result of a kick on the football field, received 200 grm. gelatin daily throughout the period of observation. From the sixteenth day following the injury it was omitted. From the second to sixteenth days the patient lost 15·30 grm. N. The urinary N varied with the total volume of urine passed during the gelatin feeding period, but the body temperature was never above 36·83° C. during the whole period of observation. The preformed creatinine excretion was very constant. The creatinuria was marked and its daily fluctuations corresponded with the changes in total urinary N. On ceasing to give gelatin it quickly declined, and within three days only a trace was present.

The most marked creatine excretions of the series were noted in these two cases and in *Case* 6, who received 10 grm. glycine daily. The degree of creatinuria in the former two cases appeared to be definitely related to the ingestion of gelatin, and since glycine itself appeared to produce a similar effect it may be reasonable to assume that the increased creatinuria induced by gelatin feeding was related to its high glycine content.

Many years before, Gibson and Martin (1921) had noted that the administration of gelatin to cases of muscular dystrophy led to a creatinuria. These observations in injured subjects suggest that their muscular function is deranged in some peculiar way. It has long been known that fracture cases frequently exhibit a creatinuria.

The Effect of Sodium Caseinate (175–200 grm. ' Protosol ' daily) when added to Diets of Very Low First-class Protein Content (*Cases* 11–17).— *Case* 11 received his injuries—a fractured humerus at the junction of the upper
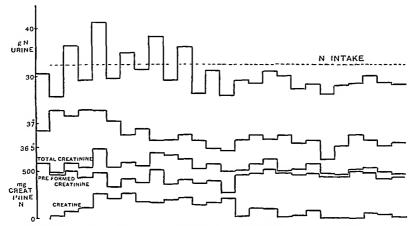
Fig. 342 —*Case* 11   Daily fluctuations in average body temperature, urinary N, and total creatinine, preformed creatinine, and creatine (expressed as creatinine N).

and middle thirds, with bruising plus a lacerated wound over the right supra-orbital ridge—as the result of colliding into a wall when bicycling. His arm was massaged daily and gently moved before being put back into the splint. For the first week he stayed most of the time in bed as his body temperature was slightly above 37° C. for some six days. The patient lost 13·75 grm. in twenty-three days. The main loss of substance took place during the first ten days, when

39·59 grm. N were excreted in excess of intake, and from the fifteenth to twenty-seventh days 25·84 grm. N were retained. In addition to a diet low in first-class protein he consumed 175 grm. 'Protosol' daily.

The urinary volume fluctuated with the N excretion, but later continued to rise as the N gradually fell. The urinary N and the body temperature curves were parallel, the daily fluctuations corresponding (*Fig.* 342). Preformed creatinine fluctuated with the urinary changes, but as the urinary N rose the preformed creatinine decreased slightly, rising again as the urinary N fell. Creatine excretion rose from zero, then remained parallel to the total urinary N, and finally declined as the latter fell, becoming eventually little more than a trace. The degree of creatinuria is apparently related to the total protein catabolism, and this experiment would suggest that as this creatinuria waxes the preformed creatinine output wanes slightly.

The basal diets of *Cases* 11 and 12 were creatine- and creatinine-free.

Case 12 received 200 grm. sodium caseinate daily during his convalescence from the fracture of both bones of one leg at the mid-point caused by a direct blow by a machine handle. The wound, which was compound, was incised and cleaned under chloroform and ether anæsthesia. No sepsis resulted. During nine days the patient lost 50·88 grm. N. The urinary volume rose with increase in N excretion and continued rising even after the N had reached its maximum value. The maximum body temperature (37·44° C.) coincided with the maximum N excretion. Preformed creatinine remained fairly constant, though as in the previous case a tendency to fall as the creatinuria developed was noted. The latter initially varied with the total N excretion, but later fell although the N output still remained high.

Case 13 had the lateral and medial malleoli of the bones of one leg fractured as the result of a wagon passing over his leg just above the ankle. Though the diet contained 23·82 grm. N daily, the patient during seven days of observation lost 36·79 grm. N. Total urinary S fluctuated in parallel with total N and urinary volume. As no precaution had been taken to prevent S loss in the fæces during drying, only the excess outputs of N and S in the urine can be compared. On this basis the S : N ratio of the material lost was 1 : 16·36. The S : N ratios of intake and total urinary outputs were 1 : 13·65 and 1 : 13·79 respectively. The S : N of the urinary excretions during the first and second periods of five days were 1 : 13·63 and 1 : 13·94 respectively. The excretion of preformed creatinine rose slightly, the rise corresponding to the rise in total N. The creatinuria diminished slightly. Owing to the fact that the patient was on a meat-containing diet little value can be attached to this apparent reciprocal relationship.

In this case there was practically no disturbance of body temperature.

Case 14 received a compound fracture of both bones of one leg (fracture at the mid-point) as the result of having his leg crushed between two large drain pipes. During the period of observation (thirteen days) he lost 27·26 grm. N, the daily intake being 26·57 grm. The excretion of total S in the urine varied with that of total N and the volume of urine passed showed similar changes though occurring somewhat later.

The maximum values for the oxygen consumption, body temperature, and pulse-rate coincided in time with the maximum excretions of N and S in the urine, and the trend of all these values was in the same general direction—

namely, an irregular rise to a maximum on the seventh day and an irregular fall thereafter. The respiratory quotient varied between 0·76 and 0·85 during first twelve days ; thereafter it gradually rose to 1·15. The output of preformed creatinine was fairly constant; such variations as occurred were parallel to the general trend of N and S. The degree of creatinuria was slight and remained practically constant throughout the period of observation.

The fall of a coal tree fractured both bones of both legs of *Case 15.* Both bones of the right leg were fractured about the middle, those of the left leg at the junction of the proximal and second quarters. During the ten days of observation he lost 17·59 grm. N even though on a diet of high first-class protein content
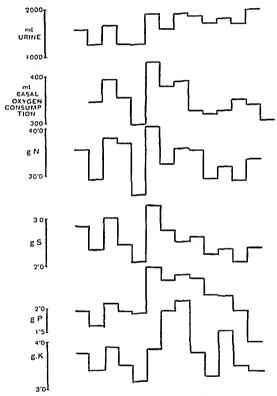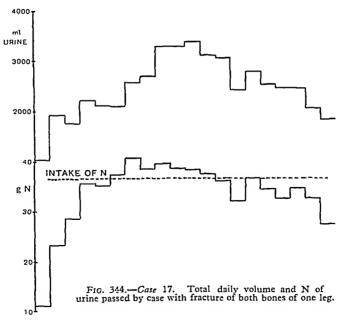
FIG. 343.—*Case* 15. Daily basal oxygen consumption, volume of urine, and urinary output of N, S, P, and K, following the fracture of both bones of both legs.

(31·84 grm. N daily). The urinary volume, total N, total S, total P, and to slightly less extent K, exhibited similar daily variations (*Fig.* 343). The values did not show the characteristic slow rise to a maximum and subsequent gradual fall noted in most of the other cases. The daily fluctuations in the excretion of these catabolites were paralleled by similar fluctuations in the basal consumption of oxygen, body temperature, and pulse-rate, indicating that these irregularities were not simply variations in the daily excretion but due to differences in the rate of metabolism. The excretion of preformed creatinine remained remarkably constant;

such fluctuations as occurred corresponded with those of the other urinary catabolities. The creatinuria gradually rose to a maximum on the eleventh day following the injury, then declined.

As the result of being charged by an opponent when playing football *Case* 16 fell heavily to the ground, both bones of one leg being splintered at their mid-point. The leg was so swollen on admission to hospital that it was impossible to put it in a splint. For five days it lay between sand-bags. It was then manipulated and splinted. Six days later a pin had to be passed through the os calcis and extension applied. The leg was still considerably swollen at the site of injury sixteen days after the accident. During these two days of manipulation the intake of food was greatly diminished, 5 grm. N being consumed on the first occasion and less than 2 grm. on the second occasion. The patient lost 45·82 grm. N in the course of fifteen days. The average daily intake of N inclusive of the two days of manipulation was 33·84 grm. The surgical procedures each produced a definite but temporary increased excretion of N over and above the general rise and fall resulting from the original injury. The urinary volume and body temperature varied with the total N excretion.

FIG. 344.—*Case* 17. Total daily volume and N of urine passed by case with fracture of both bones of one leg.

Case 17 (*Fig.* 344), the last member in this group receiving high protein diets, sustained a fracture of both bones of one leg just above the ankle due to a fall of stone. The daily intake of N was 36·69 grm. (meat, eggs, and milk mainly). During the seventeen days of observation the patient stored 25·49 grm. N.

From this experiment it appears that on superimposing a diet containing the maximum amount of first-class protein which can be ingested over a period with a minimum of discomfort, upon a diet of average N content, there occurs first a period of retention while the N excretion is rising, then a period of loss, to be followed later by another period of retention. The fact that there was a loss of N during a considerable part of the period appears to indicate that in such cases

of injury attempts to stem completely the loss of body tissue fail during the period of maximum tissue catabolism.

The maximum volume of urine was passed subsequent to that of the total N.

This group of experiments indicates that in cases of fracture due to direct violence, where in addition to the breaking of bone there is a definite amount of soft tissue damage (mainly muscle) with presumably extravasation of blood, attempts to maintain these patients in nitrogen equilibrium during the period of maximum catabolism fail. The loss is less the higher the protein intake.

The caloric value of the last group of cases (*Cases* 13–17) varied between 3044 and 3606 Cals. The recorded N losses in all the cases are slightly greater than the actual, since no account has been taken of the sweat N.

The Effects of Diets of High Carbohydrate and High Calorie Content (*Cases* 18, 19).—In consideration of the sparing action of carbohydrate on the rate of protein catabolism *Cases* 18 and 19 were fed with mixed diets of high carbohydrate content—diets of 4135 and 3592 Cals. respectively.

Case 18 had the lower end of the left fibula fractured as the result of a fall of stone. There was practically no displacement of the fragments. In the course of nine days this man lost 35·90 grm. N (daily intake 16·39 grm. N).

Case 19 suffered from a fracture of the lower ends of both bones of one leg. The ends were manipulated into position without anæsthesia. During the course of five days the patient lost 47·57 grm. N (daily intake 8·31 grm. N).

In both cases the urinary volume varied with the excretion of N. The body temperatures did not rise concurrently with the total N. In *Case* 19 the maximum temperature (37° C.) was recorded three days after the maximum N excretion.

DISCUSSION

In the course of the foregoing experiments attempts have been made to prevent the loss of N which occurs during the period of increased catabolism that follows severe injuries due to direct violence. In the light of the data derived from patients receiving diets rich in first-class protein and of high caloric value it is obvious that no success could have attended the earlier experiments where supplements of meat extractives, certain amino acids, and incomplete proteins were given to subjects receiving diets of average or low caloric value and low in first-class protein.

From certain incomplete observations on cases of fracture due to indirect violence where little or no tearing of soft tissue had resulted from the displacement of the bone fragments, the evidence suggested that N equilibrium could be attained more easily, particularly when the cases received similar mixed diets of high protein content.

Reference to the early literature indicates that when high protein diets or low protein diets of very high caloric value are fed to normal uninjured persons, N retention may apparently occur. Krug, a pupil of v. Noorden's (q.v.), carried out experiments on himself, a healthy individual showing no sign of wasting. During a preparatory period of six days he attained N equilibrium on a diet of 2590 Cals. (44 Cals. per kilo.). On raising his intake by an additional 1700 non-protein Cals. he retained 49·5 grm. N during fifteen days, the retention being as great at the beginning as at the end. Bornstein (1898) noted a retention of 16 grm. N in fourteen days when he supplemented a diet sufficient to maintain N equilibrium with an additional 40 grm. protein. The most outstanding example of this

storage phenomenon has been described by Lüthje (1902), who noted gains of 10 to 20 grm. N daily in a subject in good condition, who consumed a daily diet of 6000 Cals. containing 380 grm. protein.   C. Voit had shown that the increased amount of flesh that is put on by the dog during a surplus diet is frequently lost on return to the normal diet.   Dengler and Mayer (v. Noorden, 1909) found that a man aged 42, previously in a good state of nutrition, gained 371 grm. N in seventy-two days when the diet was gradually raised from 2183 to 4695 Cals. and then reduced.   The maximum gain occurred during the period of maximum caloric intake.

In order to test this apparent capacity of the normal human organism to store N when placed on a high protein diet, the retentive powers of two healthy male students, H. M. and J. H., aged 19 and 23 years respectively, were examined.

Having attained N equilibrium on a well-balanced normal diet containing 16·78 grm. N, student H. M. was placed for six days on a diet of similar caloric value but containing double that amount of protein—mainly first-class (33·75 grm. N ; 2822 Cals.).

					Grm.
Daily basal intake N ..	..	..	..	..	16·78
Daily urinary N during basal intake..	..	..	..	14·90
Daily fæcal N ..	..	..	..	..	1·49
Total daily output on basal ..	..	..	..	16·39
Balance (excluding loss of N by sweat)	..	+ 0·39
Extra food N (6 days) over basal ..	..	..	101·82
Extra urinary N over basal ..	..	..	..	100·18
Balance	..	+1·64

The retention of 1·64 grm. N as the result of six days' excessive N feeding is insignificant, as it is probable that some extra N would have been excreted in the fæces and sweat during the period of high protein intake.

The second experiment (student J. H.) was unsatisfactory in many aspects, but does indicate a similar finding.

					Grm.
Basal food N (10 days)	..	..	..	..	145·7
High N diet (10 days)	..	..	..	..	324·3
Extra food N (10 days)	..	..	..	..	178·6
Extra urinary N over basal ..	..	..	..	179·0
Balance	..	−0·4

This figure (– 0·4 grm.) is negligible.

It is apparent that these two individuals did not exhibit any capacity for retaining N when placed on a high protein diet such as the fracture cases received. The writer is therefore unwilling to believe that the retention phenomena described by earlier workers is a general occurrence, though undoubtedly certain people increase in weight when their intake of food is increased, and, though this increase in weight is mainly fat, it is possible that protein may also be stored as indicated by N retention.*

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* Since this was written further experiments on student H. M. and on the writer himself indicate that when first-class protein (in the form of milk) is added to a diet adequate in calories but low in first-class protein (80 grm. protein : 23 grm. first-class) N retention occurs.

The actual fracture of bone probably causes but little disturbance, the major disturbance apparently resulting from the tearing of the soft tissues by the displaced bone fragments and from the damage done to the soft tissues by the traumatic agent itself. There appears to be no obvious relationship between the amount of damage and the catabolic response. Individuals react differently. The most severe injuries of this series were those of *Case* 15 (fracture of both bones of both legs). In this case the loss was only 17·59 grm. in ten days, the N intake being 31·84 grm. daily.

According to Linser and Schmid (1904), no breakdown of tissue protein occurs in normal persons as the result of the external application of heat if the body temperature is maintained under 39° C. Graham and Poulton (1912–13) noted no appreciable increase in N excretion as the result of raising the body temperature to 39·44° to 40° C. by exposure to steam heat. It is unlikely, therefore, that an appreciable part of the increase in catabolism observed in these injured subjects is due to the slight pyrexia sometimes found. It is much more reasonable to believe that the increase in temperature is (in part at least) due to the increased catabolism.

Absorption of digestion products from the gut cannot be appreciably affected in injury, as in only one case (*Case* 17, who received maximum protein) did the fæcal N excretion exceed an average of 2·0 grm. per day.

Several attempts have been made in the past to maintain N equilibrium at the height of an infective fever. Shaffer and Coleman (1915) believed that the lack of success lay in the fact that food of insufficient fuel value and of unsuitable character had been used. The work of Lusk (1891), Sivén (1901), Landergren (1903), Folin (1903), Murlin (1907), and others had shown the superior value of carbohydrate in sparing body protein in fever. Shaffer and Coleman were, however, able in only one instance to obtain N equilibrium in the early stages of typhoid and they were unable at any time to maintain it for more than two to three days when the temperature was above 38·89° C., although the patients were receiving as much as 90 Cals. and 1·6 grm. protein per kilo. per day. Rolland (1912) almost attained N equilibrium in febrile patients with diets high in both calories and protein, but Coleman and Du Bois (1915) failed to establish N equilibrium in cases of typhoid and other fevers on diets containing adequate calories and as much as 15 grm. N daily. Lauter and Jenke (1925) and others have also failed to establish N equilibrium in fever with diets of high caloric content.

The increased N excretion in febrile infections is due not only to the extra liberation of energy but also to an active destruction or autolysis of tissue. The failure to attain N equilibrium at the height of catabolism in the present series of cases is all the more extraordinary therefore, considering that there was little or no disturbance of body temperature.

In those subjects on whom basal metabolic determinations were made the oxygen consumption varied with the body temperature and pulse-rate, and in most cases this corresponded to the maximum period of N excretion. This period of maximum excretion was reached from the fourth to the eleventh day following the injury, generally the sixth day in this series. The amount of N excreted generally rose gradually to a maximum and then slowly declined.

The excretion of total urinary S ran parallel to the curve of N excretion in

the two cases (*Cases* 13 and 14) in which it was followed throughout the experimental period. Relative to N slightly more S was excreted in the first half of the experimental periods, which lasted ten to sixteen days respectively. The S : N ratio of the material lost by *Case* 13 was 1 : 16·36, a ratio which indicates the catabolism of muscle substance.

Although balances were not struck in the case of P, K, and Na, it was apparent that the excretion of the former two elements varied with that of N, while Na remained fairly constant. The fact that K and not Na was the variable element suggests that cellular material was being catabolized.

The fluctuations in the urinary volume were mainly dependent on variations in the rate of excretion of the products of catabolism.

Omitting for the moment those cases receiving gelatin or creatine- and creatinine-containing foods, the two cases remaining (*Cases* 11 and 12) in whom the creatine and creatinine excretions were studied exhibited creatinurias paralleling the changes in urinary N. The creatinine excretion tended to vary inversely with the degree of creatinuria. This was more noticeable in *Case* 11. The combined creatine and creatinine excretion rose and fell with the total N excretion, the fluctuations being less marked in the case of creatine alone. These increases were not due to a washing out of catabolites, for the urinary volume rose to its highest level during the period of total N and total creatinine decline. These observations suggest either that the metabolic process which has creatinine as an end product is in part arrested at the stage of creatine, or that these two metabolites have separate origins, the creatinuria arising from the breakdown of perhaps local muscular tissue, the diminution of creatinine excretion being the result of a general decline in the activity of the total protoplasmic mass following on the injury. The latter is perhaps the more reasonable explanation, but if true it would indicate that the main catabolism is local and not general, a conclusion somewhat difficult to believe in the face of the marked loss of N which may sometimes occur— 137 grm. in ten days, but yet supported by clinical evidence of localized atrophy.

In those cases receiving gelatin (*Cases* 9 and 10) the excretion of preformed creatinine was fairly constant and independent of the amount consumed. On the other hand, the creatinuria was dependent in part on changes in the intake of this protein, for, on increasing or decreasing the amount taken, similar changes occurred in the amount of creatine excreted. The level of the creatinuria in these two cases and in those receiving glycine was the highest of the series, though never exceeding 650 mgrm. (in terms of creatinine N), and, in those cases receiving creatine- and creatinine-containing foods (*Cases* 5, 14, and 15), the degree of creatinuria was often very constant and generally of a lower value than was observed in the other cases.

So far it has only been possible to trace the fate of the nitrogen and sulphur residues of the protein which has been catabolized.

No account has been taken of the deaminized residue or of the contemporaneous catabolism of carbohydrate and fat reserves. If oxidation of the substances is in excess of normal, then the energy liberated must appear as heat or work. That there is an increase in the oxidative processes of the body is certain, and that the slight rise of body temperature is not a sufficient explanation of the manner in which the liberated energy is expended is also certain. Of work done we have no knowledge except that the ordinary processes of healing will require a greater

expenditure of energy than normal for the synthesis of new tissue and for the removal of effete material. Therefore, although this excessive catabolism which follows severe injury caused by direct violence persists in the face of what is probably the maximum protein and caloric intake that the human organism can consume when confined to bed, it is modified to a considerable extent by such diets. A somewhat similar dietary effect has been noted in the case of the infective fevers. Whether the primary demand is for essential amino acids to repair the damaged zone or for fuel, it is impossible to state accurately; probably both are required, for in the two cases (*Cases* 18 and 19) which received diets of high caloric value but of average or low protein content little success was achieved.

Disuse atrophy, though a contributory factor, does not form an adequate explanation of this strange phenomenon, as the loss of body substance is greatly in excess of that produced by experimental disuse (Cuthbertson, 1929). It has long been known, however, that muscular wasting associated with bone or joint disuse is much more rapid and extreme than that which occurs with simple disuse of a limb. It is also true that there is a more rapid and extreme wasting in limbs immobilized for some inflammatory or traumatic lesion than in limbs immobilized to correct a deformity. The reason for this lies not in the degree of immobilization but in a reflex trophic effect affecting certain groups of muscles more than others in the same region. Such reflex atrophy is dependent on the integrity of the afferent nervous paths (Harding, 1925, 1926, and 1929).

One is tempted to speculate that herein may lie an explanation for this trophic change, the resultant rapid wasting of muscle being the response to the organism's urgent demand for material for maintenance and repair. As was suggested in an earlier paper (Cuthbertson, 1930) injury to an animal generally leads to lessened activity and a lessened activity to a diminished food supply. The necessity is urgent and the body may require and may prefer to catabolize its reserves to meet the exigencies of the moment. These experiments offer no direct evidence whether the wasting of the specific groups of muscles has in any way been mitigated by diet. Such may be the case. On the other hand, the local loss of substance may have proceeded unabated by such dietary measures, though to a great extent masked by anabolic processes proceeding elsewhere. Further experiments are required to elucidate this very interesting point.

Be that as it may, the beneficial effect of a diet of high protein and caloric content in diminishing this wastage of flesh that generally follows injury due to direct violence is sufficient to warrant the provision of such diets to injured patients. Accident cases can generally tolerate and even enjoy such diets and we have not found that they retard the healing of bone. It is probably advisable to supplement such high protein diets with a certain amount of base contributing foodstuffs—viz., vegetables and fruit.

SUMMARY

1. The ingestion of diets very rich in first-class protein and of high caloric value by persons suffering from the fracture of one or more of their long bones as the result of direct violence, modifies considerably the marked loss of body protein which normally occurs under such circumstances. At the height of the catabolic disturbance, however, such diets still fail to prevent this loss of protein.

2. Measures such as massage and manipulation, the addition of meat extractives, glycine, hydrolysate of mixed ox tissue, gelatin, and sodium caseinate, and diets of high caloric value but average protein content, similarly failed to stem the loss of protein and generally proved less successful in mitigating the drain on the body's reserves.

✓ 3. The catabolic disturbance is characterized by an increase in the basal consumption of oxygen with attendant rise in pulse-rate and temperature, and by parallel rises in the urinary output of N, S, P, and to a less extent K.

✓ 4. The creatinuria which develops and parallels the rise in total N is accompanied by little change in the creatinine excretion; such change as occurred took the form of a slight diminution during the period of maximum creatinuria.

5. Two control subjects who received diets rich in first-class protein and of high caloric value exhibited N equilibrium.

6. It is recommended that injured patients should receive diets of high protein and caloric content.

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ŒSOPHAGECTOMY FOR CARCINOMA OF THE THORACIC ŒSOPHAGUS

By E. S. J. KING

SURGEON TO OUT-PATIENTS, ROYAL MELBOURNE HOSPITAL, MELBOURNE

Of all the conditions that are difficult of treatment because of their nature or inaccessibility, carcinoma of the thoracic œsophagus has seemed to be one of the least amenable to successful surgical attack. As Grey Turner[11] has said, it " has usually been considered the most unsatisfactory subject in the whole realm of surgery ". Nevertheless in the last few years a number of cases successfully treated* have been reported by Torek,[10] Lilienthal,[9] Eggers,[1, 2] and Grey Turner.[12] The pioneers, Mickulicz, Richter, Quénu and Hartmann, Rehn, Enderlen, and Sauerbruch amongst others, whose work undoubtedly paved the way for the subsequent successes, deserve more than a passing thought for a courage, determination, and enterprise that is seldom required of modern surgeons. Nevertheless success does capture the imagination, and Torek's[10] transpleural œsophagectomy in 1913 will remain one of the outstanding feats of surgery. Since then Eggers[1, 2] has had, by this method, two successful cases. Lilienthal[9] performed an œsophagectomy by the posterior mediastinal route. By a modification of a method unsuccessfully used by Teutonic surgeons,[4, 8] Grey Turner[11, 12] recently has had a successful case.

A number of successful operations for carcinoma of the lower end of the œsophagus or the cardia of the stomach, and for non-malignant tumours, have been recorded (Gohrbandt,[5] Hedblom,[6] Krauss,[7] Voelcker,[13] Zaaijer,[14] amongst others), but these need not be discussed here.

The following is the report of a case in which a satisfactory result has been obtained.

CASE REPORT

Mrs. B. K., aged 56 years, had had dysphagia for eight months. This had been worse for the last two months, so that for two or three weeks she had been able to swallow only fluids. There had been no pain in the chest.

X-ray examination (barium swallow) revealed an obstruction of the œsophagus opposite the junction of the sixth and seventh thoracic vertebræ (*Figs.* 345, 346). Œsophagoscopy, performed by Dr. A. Blaubaum, revealed a mass projecting into the œsophagus and constricting it, 12 in. from the incisor teeth. A portion of the mass was removed, and on microscopical examination this showed an epidermoid carcinoma.

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* ' Success ' must of necessity be a relative term when dealing with malignancy. Torek's case is actually the only one in which the disease was completely eradicated, his patient living for thirteen years. However, the operative successes give promise of hope for cases which are diagnosed sufficiently early.

The patient and her relatives were informed of the diagnosis and of the risks of surgical intervention and were agreeable for any treatment to be adopted. She was admitted to the Royal Melbourne Hospital on Feb. 21, 1935. Her general condition was good except that there was pyorrhœa round some of her lower teeth. Her renal function was satisfactory and the lungs were clear. The Wassermann reaction was negative. Her weight was 7 st. 6 lb., about a stone below her normal weight.

Gastrostomy (Senn) was performed under local block anæsthesia on Feb. 22. Convalescence was satisfactory except that, on the day following operation, the patient vomited, apparently as the result of a morphia idiosyncrasy. Omnopon was used during the remainder of her stay in hospital.

FIG. 345.—X-ray photograph of the chest showing the obstruction in the œsophagus opposite the junction of the sixth and seventh thoracic vertebræ.

FIG. 346.—Obstruction to the œsophagus shown in oblique view after administration of a thin meal.

Energetic treatment of the mouth condition had been adopted, though the teeth were not removed. She was given a high caloric diet, with adequate vitamin content, through the gastrostomy tube (three-hourly feeds). Artificial pneumothorax of the left side was produced by injection of increasing amounts of air on each second day.

Five days later (Feb. 27) under gas and oxygen anæsthesia, through a paravertebral incision, the vertebral ends of the 4th, 5th, and 6th ribs on the left side were cut and the intercostal vessels and nerves were ligated and cut. The wound was then sutured. The patient recovered from this procedure uneventfully and as her general condition was good it was decided to proceed with the œsophagectomy.

Three days later (March 2) œsophagectomy was performed. Under avertin and intratracheal gas and oxygen anæsthesia, with the patient in the right lateral position, an incision was made along the sixth intercostal space, this incision connecting at its vertebral extremity with the lower end of the paravertebral incision previously made. The muscles (trapezius and latissimus dorsi) were incised and hæmostasis obtained. The wound made at the preliminary operation in the trapezius and rhomboids, on the medial aspect of the scapula, was opened up. The intercostal muscles of the sixth space and the underlying pleura were now incised and the incision in the pleura continued upwards, at the vertebral end, to the 3rd rib.

A rib-spreader was introduced and a clear view of the pleural cavity obtained. The lung was collapsed against the mediastinum and there were about 4 oz. of slightly blood-stained fluid in the cavity. The fluid was aspirated. The hilum of the lung was normal and no nodules could be felt in the lung tissue. One fairly dense adhesion was present between the apex of the lung and the parietal pleura. This was divided.

An incision was then made in the mediastinal pleura, just in front of the descending aorta, from the diaphragm to the arch of the aorta, and a further one, in line with this, from the arch to the cupola of the pleura.

The mediastinal tissues in the lower part were dissected, partly by sharp and partly by blunt dissection, and the œsophagus freed so that a tape could be passed round it, and separated upwards and then downwards from this point until it was free in the whole of its extent from the diaphragm to the arch. The major vessels were grasped by forceps, cut and then sealed with the electric cautery. Both vagi were cut across sharply opposite the left bronchus, at an early stage of this procedure. This did not cause any appreciable alteration in pulse-rate or blood-pressure. The tumour was found just below and partly behind the arch of the aorta and appeared not to have infiltrated the surrounding structures.

Dissection of the mediastinum above the arch of the aorta was now undertaken and the œsophagus freed down to and around the tumour. Attention was then directed again to the œsophagus below the arch. It was drawn out and moist gauze was placed in the œsophageal bed. The upper part of the stomach was drawn slightly through the diaphragmatic opening and a purse-string suture was placed in its upper part so as to surround the œsophagus. The lower end of the œsophagus was tied in two places with heavy silk and was cut across with the electric cautery. The lower end was invaginated into the stomach and the purse-string tied. A second purse-string was introduced into the diaphragm just peripheral to the first one, and also tied.

The upper cut end was covered by a rubber sheath, which was tied on by two separate ties at an interval of an inch, to prevent leakage of infected material from the cut end on to the mediastinal surface. The œsophagus was then brought round the arch of the aorta so that it hung from the upper part of the mediastinum into the pleural cavity.

The wound was then closed temporarily and an incision was made in the neck along the anterior border of the sternocleidomastoid in its lower portion. Dissection was carried posteriorly down to the œsophagus and along this into the superior mediastinum until the cervical and thoracic dissections were joined. The chest wound was then re-opened and a pair of forceps passed into the neck wound and

down into the mediastinum until it could be seen in the chest. It was thus possible to grasp the more distal tie on the œsophagus and to draw this tube into the neck.

A drainage tube was passed through the eighth intercostal space in the posterior axillary line. The chest wound was then closed. The mediastinal pleura was left unsutured, intentionally, in order to allow drainage.

The œsophagus was then inspected and the site of division was determined. An incision was made in the skin just below the clavicle, and the subcutaneous tissues were tunnelled from the incision in front of the sternocleidomastoid to the lower incision. The œsophagus was brought through this tunnel, sutured to the skin edges, and the protruding portion (containing the tumour) was then removed by incision with the electric cautery. A few interrupted sutures were introduced to unite the mucosa to the skin. A small drainage tube was passed into the upper mediastinum through the main neck wound, which was then sutured. Dressings were applied and the patient returned to bed. The drainage tube in the chest was connected with a negative pressure apparatus. A transfusion of a pint of blood was given and saline administered by the subpectoral route and glucose-saline as a continuous rectal infusion.

Two hours after the operation the patient had a pulse-rate of 132. She seemed comfortable and was given injections of omnopon at intervals as required. Her temperature rose to 103° in the evening.

On the following day the patient looked remarkably well, though her respirations were somewhat laboured—jerky and grunting in type. Her pulse-rate ranged from 120 to 140, and in the evening her temperature rose to 104°. In the twenty-four hours after operation 18 oz. of fluid had drained from the left pleural space. Clinical examination, advisedly cursorily performed, showed the left lung to be expanded. There was a considerable amount of mucous blood-stained discharge from the opening of the œsophagus.

On the second day after operation the respirations were much easier. The pulse-rate varied between 120 and 130. The temperature was 102°. The drainage from the chest had been only 3 oz. in the twenty-four hours. There was less discharge from the œsophageal opening. The drainage tube was removed from the neck, and the sutures in the neck wound were removed.

On the third day the patient was progressing well. As there had been no discharge from the chest during the preceding twenty-four hours the drainage tube was removed. She was allowed to swallow water, this being caught in a basin. From this time the œsophagus remained clear (except for the normal discharge of saliva), and the terminal portion healed to the skin margin rapidly (*Fig.* 347).

Two days later a rubber tube was placed in the œsophagus and connected with the gastrostomy tube so that she was able to swallow directly into the stomach. This was greatly appreciated by the patient. The tube, however, could not be left in position for more than a few hours at a time as it caused irritation of the œsophagus (*Fig.* 348).

On the seventh day she developed signs of a pleural effusion on the right side; 10 c.c. of serous fluid were aspirated, culture of which gave no growth of organisms. The signs in the chest rapidly disappeared. X-ray examination of the chest on the ninth day showed the lungs to be clear and to fill the pleural cavities completely. The ribs which had been cut were in apposition (*Fig.* 349).

FIG. 347.—Photograph of the patient taken about three weeks after the operation showing the œsophageal stoma thoroughly healed to the skin.

FIG. 348.—Photograph of the patient showing the tube connecting the œsophageal opening to the gastrostomy tube.
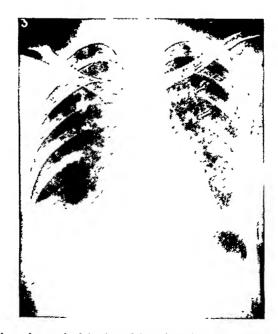
FIG. 349.—X-ray photograph of the chest of the patient taken nine days after the operation. The left lung is well expanded. There is some thickening at the site of the drainage wound. The arrows indicate the cut ribs (4th, 5th, and 6th), which are in apposition.

She was allowed out of bed on the tenth day, and from then she progressed without further complications. The wound in the chest was by this time soundly healed and the sutures were removed.

Although the general condition was improving markedly, the patient did not put on weight. It was thought that this might be due to the loss of saliva during the time when the rubber tube was not in position. A celluloid cup which had an outlet at the lower end was devised. This was placed over the œsophageal opening and the lower end connected by means of a tube with the gastrostomy. In this way she was able to obtain the greater part of the saliva escaping from the œsophageal opening. From this time she rapidly gained her normal weight.
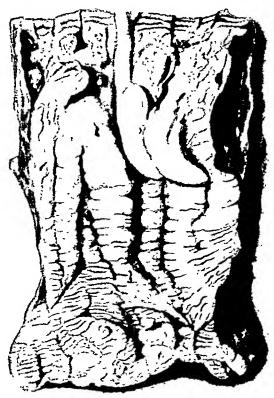
FIG. 350.—Drawing of the œsophagus after removal. The growth is of the constricting variety with but slight superficial ulceration. The specimen, which measured just under 3 in., corresponded to about 6 in. of the œsophagus (*see* text). Note the marked wrinkling of the mucosa. The raised area running from the tumour to the upper cut edge was shown to be a leucoplakic band.

PATHOLOGICAL EXAMINATION.—Macroscopically, the specimen consists of a piece of œsophagus $2\frac{7}{8}$ in. long containing a mass in the upper (cranial) portion. The adventitia of the tube is uniform in texture and is not obviously involved by tumour.

After splitting the tube the mucosa of the lower part is seen to be normal showing a marked transverse wrinkling (*Fig.* 350). A thickening of $\frac{1}{4}$ to $\frac{1}{2}$ in. extends for $\frac{7}{8}$ in. along the wall, the upper extremity of this being within $\frac{1}{4}$ in. of the upper edge of the specimen. This cut margin appears to be normal.

A linear whitish band suggesting leukoplakia extends from the tumour up to the line of the incision.
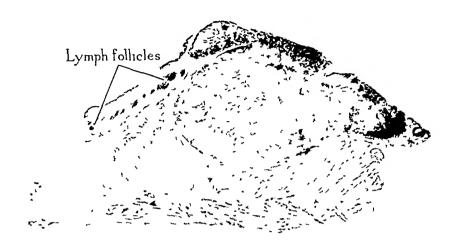
FIG 351 —Low-power photomicrograph of the tumour, which is well circumscribed and has not invaded the adventitia of the tube. (× 4)

(*Note.*—The actual length (2⅞ in.), as compared with the original length of œsophagus removed (about 6 in.), and the small distance (¼ in.), as compared with 1 in. of apparently uninvolved œsophagus observed at operation, are due to the contraction of the longitudinal muscle as shown by the transverse wrinkling).

Microscopically the tumour mass is fairly circumscribed in all the sections examined, extending into the muscle coat but not into the adventitia (*Fig.* 351). The tumour is a squamous-cell carcinoma. Groups of cells showing intercellular prickles are closely arranged in a very small amount of connective tissue. In many areas the cells are large and show early keratinization (*Fig.* 352), but no definite cell nests are present. The cell nuclei show considerable irregularity in size, but only occasional mitotic figures are to be seen.

FIG 352 —Photomicrograph of the tumour showing the epidermoid nature of the carcinoma (× 160)

There is a well-marked inflammatory condition in the tissues at the edge of the growth.

Above the tumour the œsophageal wall shows a marked degree of subacute œsophagitis. On the surface the epithelium shows marked hyperplasia, though the changes in this (which are probably only irritative) rapidly diminish until at the upper end the epithelium shows only some thickening and keratinization on the surface. In the submucous layer of this region there is some invasion by epithelial cords, but this extends for a short distance in a cranial direction. On the caudal side of the tumour the epithelium becomes normal more abruptly. There are some lymphoid accumulations (*Fig.* 351) in the submucous layer, but otherwise little evidence of inflammation.

SUBSEQUENT COURSE.—The patient is now very well and in good condition. There is no evidence of recurrence or metastasis. An œsophagoplasty is being undertaken and will be reported later.

DISCUSSION

A number of principles have emerged from the available mass of experimental observations, clinical investigation, and operative endeavour. These are that : (1) Cognisance must be taken of the special physiological peculiarities of the region attacked ; (2) Changes brought about in organs should, where possible, be gradual ; (3) The œsophagus must be removed entirely from the thorax and especially from the mediastinum ; (4) Special care must be taken to avoid infection of the pleura and the mediastinum.

1. The negative pressure of the thoracic cage has always been one of the essential problems of surgery of the thorax. Many attempts have been made to overcome the difficulty by extrapleural approach to the œsophagus. As this gives inadequate exposure, the pressure chambers used by Sauerbruch were invented to overcome the difficulties. The introduction of intratracheal anæsthesia has been a further advance. Now, however, using an apparatus which delivers gas through a well-fitting mask at a slight positive pressure, even the intratracheal tube may be dispensed with.

At the end of the operation special arrangements must be made to restore the original conditions as far as possible. How satisfactory this may be is shown in *Fig.* 349, where the left lung is seen to be completely expanded and apparently normal a few days after operation. Clinical examination had shown it to be filling the chest the morning after operation. The procedure of applying slight suction automatically solves the problem of drainage of the chest, which, as shown by Eggers,[3] is an essential part of the after-treatment.

2. In transpleural approach to the mediastinum, the sudden collapse of the lung with sudden alterations in vital capacity, disturbance of blood distribution, and movements of the mediastinum, all place an unnecessary burden on an already over-strained patient. The preliminary induction of a pneumothorax overcomes these troubles.

3. Almost all attempts to anastomose the ends of the œsophagus in the mediastinum have been unsuccessful. Not only would the excision of a small piece of œsophagus be inadequate from the point of view of cure of a cancer, but this part of the alimentary canal has no cœlomic covering, and leakage is almost inevitable.

Another point which apparently is not generally appreciated is that the longitudinal muscle of the œsophagus is in a state of considerable tension. This is demonstrated by the remarkable shortening of the organ when it had been cut across. The piece of œsophagus removed in this case extended from a short distance above the diaphragm to above the arch of the aorta (at least 6 in.) and yet the specimen now measures about 3 in. (*see Fig.* 350).

It should be mentioned that anastomoses between stomach and œsophagus in the lower mediastinum have been performed.

4. The necessity for special care with regard to prevention of infection is apparent from the many observations that the majority of cases operated on die from mediastinitis or pericarditis within a few days of the procedure. Not only must all care be taken to avoid infection at the operation, but prophylaxis by thorough cleansing of the oral cavity should be undertaken. The importance of this procedure is shown (if such, indeed, is necessary) by the observation that edentulous patients may survive a perforation of the œsophagus, e.g., by foreign bodies, whereas those with pyorrhœa or other mouth infections seldom do.

It is not proposed to discuss here the relative merits of transpleural and the varous extrapleural approaches, though I am personally convinced of the superiority of the former method.

The success of this case was due, in no small measure, to the close attention to detail paid by my house surgeon, Dr. E. E. Dunlop. It is with pleasure also that I record my appreciation of advice with regard to certain technical details given me by Mr. G. Gordon-Taylor when he was in Melbourne in November, 1934.

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GASTRIC DIVERTICULA, WITH REPORT OF A CASE BEFORE AND AFTER OPERATION

By G. A. EWART

SURGEON, ST. GEORGE'S HOSPITAL, LONDON

AND G. R. MATHER CORDINER

ASSISTANT RADIOLOGIST, ST. GEORGE'S HOSPITAL, LONDON

ALTHOUGH regarded as a rarity, a diverticulum of the stomach is commoner than is generally supposed. In a series of 370 consecutive opaque-meal examinations a gastric diverticulum was found in 11 cases. This series included a case of a post-operative diverticulum following a wedge excision of an ulcer on the lesser curvature. Excluding the post-operative diverticulum, so far only one of the cases has been confirmed at operation. The following is a short account of the case.

CASE REPORT

The patient, a man of 34 years, a dispenser at a London hospital, had suffered from indigestion for several years, gradually getting worse during the past two years. In character the indigestion was suggestive of a duodenal ulcer, there being marked hunger pain relieved by taking food. There had never been vomiting, hæmatemesis, or melæna. After self-treatment for some months with various alkalis, the patient eventually consulted the resident assistant physician. Physical examination was negative and the patient was referred for X-ray examination for duodenal ulcer.

X-RAY REPORT (*Figs.* 353, 354).—There is a pouch-shaped projection from the posterior wall of the stomach in the neighbourhood of the cardiac opening. The pouch is connected to the stomach by a stalk, passing into which are mucosal folds. These folds are continuous with the mucosal folds of the stomach. The pouch is situated under cover of the ribs and is not accessible to palpation. A large residue remains in the pouch after the stomach is empty and the residue persists in the pouch for twelve days. There is no ulcer niche in the stomach or duodenum and there is no other lesion detected in the remainder of the alimentary tract.

DIAGNOSIS.—Gastric diverticulum.

PRE-OPERATIVE TREATMENT.—The patient was kept in bed for a week. The diet was restricted mostly to fluids, and large quantities of glucose were given.

OPERATION (G. A. Ewart).—The abdomen was

FIG. 353.—Residue present in diverticulum twelve days after meal. None of the second opaque meal, given in the erect position, has entered the diverticulum.

opened through the left upper rectus muscle. On examination it was found that the liver and stomach were rather low in position, the latter being contracted and free of gas—probably the result of the careful preparation of the patient during the previous week.

Examination of the stomach and duodenum showed no sign of ulcer. The method of approach had been previously discussed with Sir Thomas Dunhill, whom I have to thank for his help. His suggestion was to divide the 6th and 7th costal cartilages near the sternum if additional exposure was required. This, however, did not seem necessary owing to the relatively low position of the stomach. An incision was next made in the gastro-hepatic omentum and vessels were ligatured.

The lesser sac of peritoneum proved to be almost obliterated by fine filamentous adhesions. Palpation in the supposed position of the diverticulum failed to give any indication of its presence. After a tedious and somewhat *anxious period of gauze dissection, the fundus*
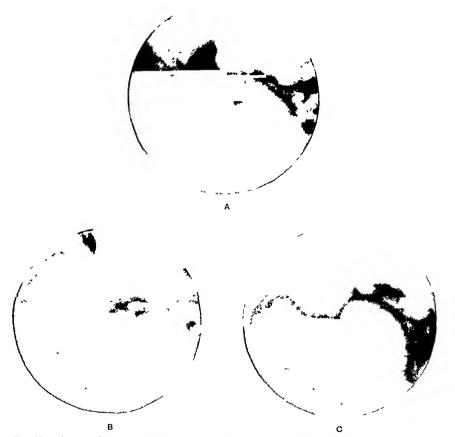
FIG. 354 —A series of aimed exposures showing the diverticulum : A, Postero-anterior view ; B, Oblique view, showing mucosal folds entering stalk , C, Lateral view, showing the stalk.

of the diverticulum was eventually discovered, lying in close proximity to the descending aorta. The fundus was grasped with a pair of sponge forceps and the diverticulum freed of its surrounding adhesions. When thus displayed the diverticulum was about $2\frac{1}{2}$ in. long, rather like the thumb of a glove (*Fig. 355*). The thin stalk shown on the radiograms was not seen. The neck of the diverticulum was next crushed and ligatured, and eventually buried with a purse-string suture, and finally oversewn with a series of sero-serous sutures. The abdomen was then closed without drainage.

SUBSEQUENT PROGRESS.—The patient made a good recovery and had a comparatively uneventful convalescence. Since operation, twelve weeks ago, he has been quite free from

his previous indigestion and has gained 11 lb. in weight.   He volunteers the fact that he has never felt so well in his life.

PATHOLOGICAL REPORT (Dr. John Taylor).—A section of the diverticulum shows that all the coats of the stomach are present.

A further X-ray examination shows that the stalk of the diverticulum is still present in the wall of the stomach (*Figs.* 356, 357).

FIG 355.—Appearance of diverticulum at operation.
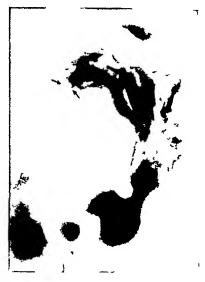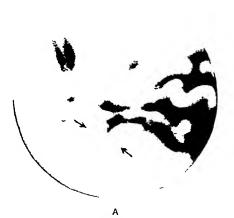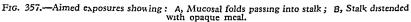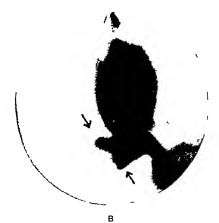
FIG. 356.—After operation, showing diverticular stalk.

A

B

FIG. 357.—Aimed exposures showing :   A, Mucosal folds passing into stalk ;   B, Stalk distended with opaque meal.

COMMENTARY

Two types of diverticula of the stomach are described—(1) congenital, and (2) acquired.   True congenital diverticula are composed of all the coats of the stomach wall—mucous, submucous, muscular, and serous.   Very few diverticula have been described as present in the new-born infant or in children, either at post-mortem or radiologically.   It is therefore probable that they are extremely

rare. Diverticula in which the muscular coat is absent are classified as acquired. These represent the great majority and are found in early and later adult life. Most of them are regarded as hernial protrusions of the mucous and submucous layers at a congenitally weakened site in the muscular coat, covered by the serous layer. A few are obviously traumatic in origin, such as the post-operative diverticulum, but these are uncommon.

As regards the acquired diverticula, the prevailing view is that the most important predisposing factor is a congenital weakness or defect in the muscular coat. Diverticula are found in those situations where the muscle fibres are more widely spaced—in the region of the cardia and at the pylorus. Of other factors, that of pulsion is the most important. A herniation of the mucous and submucous coats takes place at the congenitally weakened site as the result of recurrent increases in the intragastric pressure. Once the protrusion has taken place it increases in size as the result of the repeated filling and distension which takes place with every meal. The distension leads eventually to a thinning of all the coats of the diverticulum.

The opening of the diverticulum into the stomach varies considerably, for it may be large enough to admit one or two fingers or it may be filiform in size. The size of the opening is therefore of some importance, for the smaller the opening the greater is the liability to retention of food and the development of complications. Further, the opening may be narrowed as the result of inflammatory swelling of the mucous membrane surrounding it. When a retention persists in a diverticulum, decomposition takes place and inflammatory changes supervene. As the inflammation spreads through the walls of the diverticulum, adhesions between it and neighbouring structures result from the peridiverticulitis. In these cases traction will play a part in accentuating the diverticulum.

Gastric diverticula give rise to no characteristic clinical picture, and in the living person the diagnosis can only be made radiologically. From a consideration of the ten cases it will be observed that the radiological examination was undertaken for one of three reasons : (1) Suspected gastric ulcer (4 cases) ; (2) Suspected duodenal ulcer (4 cases) ; (3) Hæmatemesis (2 cases).

In the first group a gastric ulcer as well as a diverticulum was found in 2 cases. In the second, a duodenal ulcer as well as the diverticulum was found in 1 case. In the third group no lesion other than the diverticulum could be detected. Thus in 7 of the 10 cases under consideration, the diverticulum could be regarded as responsible for the patient's symptoms.

Gastric diverticula are single and vary in size from that of a pea to a plum. They are usually to be found in the region of the cardia, most commonly springing from the posterior wall, but they are found in other situations, although less commonly so—near the pylorus (*Fig.* 358) and on the anterior wall (*Figs.* 359, 360).

Akerlund[1] in 1923 described the diverticulum at the cardiac end of the stomach as a circumscribed, rounded, bag-shaped, projection from the lumen of the stomach, showing varying degrees of distension and filling, and with an absence of radiographic evidence of an infiltrative process in its neighbourhood. When distended it has sharply defined margins and according to the degree of distension its outline may be smooth or lobulated. In the erect position it may show a fluid level, the opaque meal collecting in the lower part of the pouch and the upper part containing air. Diverticula in the region of the cardia are protected by
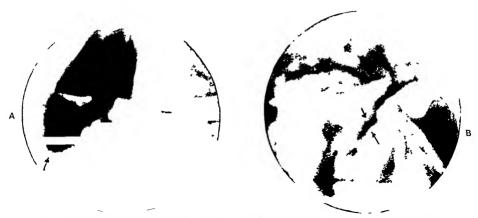
FIG. 358.—Diverticulum of pyloric canal.   A, Filled stomach ; B, Aimed dosed compression exposure showing mucosal relief of diverticulum, and mucosal folds of stalk.

FIG. 359.—Diverticulum of anterior wall of stomach.   Upper arrow indicates ulcer niche.
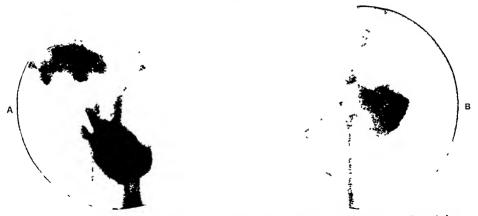
FIG. 360.—Aimed dosed compression exposures of same case.   A, Postero-anterior view ; B, Lateral view.

the ribs and are not accessible to palpation. A diverticulum arising from the anterior or posterior wall will be very easily missed if the examination is only carried out in the erect position and with distended filling of the stomach. By using small amounts of opaque meal and by examining the patient in all positions between the Trendelenburg and the erect, the diverticulum can be projected clear of the stomach, and its stalk and point of origin shown. Radiographically diverticula invariably show a stalk, although the stalk may not be apparent at operation or even at post-mortem. The stalk is situated within the wall of the stomach, and on the radiogram it is accentuated by the weight of the barium-filled pouch. At operation and at post-mortem, when the diverticulum is empty and its walls are collapsed, the stalk will not be visible. For the same reason the diverticulum itself may be very difficult to find. Berg[2] and Albrecht[3] have pointed out that in the stomach, as elsewhere in the alimentary tract, longitudinal mucosal folds enter and pass through the narrow stalk. The presence of the longitudinal folds in the stalk is pathognomonic of a diverticulum.

FIG. 361.—Gastric diverticulum, simulating a post-cardiac recess. Lower arrow indicates gastric ulcer.
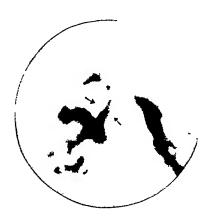
FIG. 362.—Aimed dosed compression exposure, oblique view, showing stalk of diverticulum and mucosal relief of pouch.

A gastric diverticulum may be mistaken for a large ulcer, particularly a penetrated ulcer. A diverticulum is, however, usually found in a situation where ulcers are rare, and in its immediate neighbourhood there are none of the characteristic changes which are found with an ulcer—convergence of mucosal folds, or concave indentation of the adjacent profile. With an ulcer the mucosal folds converge to the margins of the crater but do not enter into it. Occasionally in the slighter forms of cascade stomach a posterior cardiac recess may simulate a diverticulum. Examination in the oblique and lateral positions and the demonstration of a stalk serves to differentiate a diverticulum from such a recess (*Figs.* 361, 362). Occasionally diverticula in adjacent portions of the alimentary tract—in duodenum and jejunum—may be projected on to the stomach and simulate a gastric diverticulum. They should offer no difficulty in diagnosis, since they can be projected clear of the stomach, and their point of origin shown.

CONCLUSION

It would appear that diverticula of the stomach are not so rare as is generally supposed. They are commonest in the region of the cardia and may be easily overlooked at the radiographic examination. A diverticulum should not be regarded as an incidental finding since it may give rise to severe hæmatemesis or to symptoms of gastric or duodenal ulcer. Mayo[4] has reported a case of a gastric diverticulum which was the site of a carcinoma. The indications for operation would appear to be the persistence of symptoms in spite of medical treatment and the persistence of a retention in the diverticulum after the stomach has emptied.

FIG. 363.—Cardiac diverticulum, showing lobulation.

FIG. 364.—Aimed exposure of same case, showing stalk and relation of diverticulum to œsophagus.

Albrecht considers that tenderness over a barium-filled diverticulum indicates the presence of a diverticulitis. *Figs.* 363, 364 show a diverticulum in the cardiac region which was accessible to palpation, was tender on pressure, and in which a considerable retention persisted after the stomach was empty. So far medical treatment has failed to relieve the symptoms.

The actual operation, more especially in the cardiac type, must always be difficult, owing to inaccessibility and the difficulty of palpation of the diverticulum owing to the collapse of its walls. Accurate localization of the diverticulum at the radiographic examination is therefore of the greatest value.

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A METHOD OF TREATING FRACTURES OF THE LOWER LIMB

USE OF A COMBINED COUNTERPOISE AND TRACTION SYSTEM WITH A THOMAS LEG SPLINT AND HINGED KNEE-PIECE ATTACHMENT *

By A. LEWER ALLEN

SURGICAL REGISTRAR, PROFESSORIAL UNIT, GENERAL HOSPITAL, JOHANNESBURG

INTRODUCTION

THE method of treating fractures of the lower limb described by Hamilton Russell[1] combines counterpoise with extension. A travelling pulley to obtain a mechanical advantage is used. The pulley also compensates for the angles assumed. In practice, however, the Hamilton Russell method is unsatisfactory. This is probably because the angle of the knee is not fixed. The weight of the limb is supported by the sling behind the knee. The weight acting at the sling will vary indirectly with the angle between the thigh and the bed. As the patient picks himself up and so alters the angle between his thigh and the bed, the change of strain at the sling is compensated for at the travelling pulley attached to the leg. This produces a further compensatory alteration of the knee flexion. Therefore the moment the patient moves, the non-fixed knee constitutes a third variable factor in the mechanism—that is, the moment the patient moves his thigh from the bed, the mechanism becomes unstable. The patient tries to allow for this instability by altering the angle of his knee voluntarily. This often produces a painful spasm, with possible displacement. Thus only when the angle of knee flexion is constant can the mechanics of the principle of Hamilton Russell be applied.

Another common method is that which applies the Hodgen principle, using a Thomas splint. Here the splint and the limb constitute an entity which is counterpoised by weights—usually hung over the back of the bed. Another distal weight applies 'extension'. There are two great objections to this method. First, the distal or foot end is, as it were, anchored by the weight, applying extension. The ring of the splint and the thigh do not move together unless a considerable upward pull is applied proximally. This often causes undue pressure of the ring behind. Secondly, the direction and the amounts of the counterpoise and extension pulls, vary with the position of the patient in his bed. When the patient gets down to the foot of the bed the counterpoise pull acts to some extent counter to the extension pull.

In treating numerous cases of fractured femurs by the Hodgen principle with a Thomas splint, it was noticed that when the counterpoise weight was applied

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to the long bars of the splint at about the point of balance of the limb, a little proximal to the knee, the patients felt extraordinarily comfortable *until* the extension weight was applied.

The method to be described here was evolved from these observations and was designed to obviate the disadvantages and to use the combined advantages of both the Hamilton Russell and the Hodgen-with-a-Thomas-splint principles.

This method embodies the following features : The limb is fastened to the splintage apparatus. The limb and the apparatus is treated as an entity. This entity is counterpoised by a system of cords and pulleys and a single weight. At the same time and by the same mechanism a pull or ' extension ' is applied in the axis of the fractured bone.

The splint with the limb is suspended so that the whole mechanism is virtually a first-class lever. The patient controls the lever by means of that portion proximal to the fulcrum. This proximal arm of the lever is made as short as possible, and its movement is also assisted by a pull transferred over pulleys, so that the patient can control the whole mechanism with the minimum of effort and the minimum excursion of movement.

The counterpoise is of a continuous and compensating nature, so that the patient may move his limb about freely without altering the position in the splint at which the fracture has been set. The patient is thus able to govern his own movements, such as are necessary for nursing, bed-pans, and so on. He can change his position in the bed with only a slight effort and may even sleep on his side without affecting the setting of the fracture.

Results so far have shown that in the fifty-odd cases so treated such a feeling of security and ease is experienced by the patient that he will allow more manipulation and moulding to be done. Consequently with this method the resulting absence of muscle spasm and manipulation possible has given a greater accuracy of anatomical reposition of the fragments. Fine adjustments and settings of angulations, rotations, or other such corrections can be made with every assurance that they will be maintained.

The system is so arranged that the resultant of all the forces and turning moments acting on the limb ' applies extension ' in the axis of the fractured bone for whatever alteration in bodily position the patient may undergo. This resultant force can be made greater than that obtained by any direct pull because : it acts indirectly on the ' distal fragment ' from many different points of application ; the principle of the travelling pulley is used in order to obtain a mechanical advantage ; the pull is constant in direction and continuous in application, in spite of the movements of the patient. Finally, no intricate or unusual apparatus is required. Adjustments can be made and kept with mathematical precision.

GENERAL DESCRIPTION OF THE SPLINTAGE APPARATUS

Terms used and Names of Integral Parts.—The terms ' distal ' and ' proximal ' will be used to designate positions nearer the foot and the head, respectively. Traction distally in the axis of the fractured bone will be called ' extension '. The terms ' upper ' and ' lower ' will be used to show vertical relations from the floor or bed. The terms ' inner ' and ' outer ' are used relatively to the sides of the injured limb. The complete splintage, counterpoise, and

traction apparatus will be referred to as the 'apparatus'. The entity of the apparatus with the limb attached will be referred to as the 'mechanism'.

The Three Components of the Apparatus.—The apparatus may be analysed into three components : (1) The splint–knee-piece basis ; (2) The suspending cradle ; (3) The combined counterpoise and traction arrangement of cords and pulleys.

1. *First Component : the Splint–Knee-piece Basis (Fig.* 365).—This consists of the ordinary Thomas traction leg splint, a hinged knee-piece attachment, and a pair of cords. The parts of the Thomas splint to be referred to are : a proximal padded ring, an inner and outer long bar, and a distal cross-bar. The junction of the long bars with the ring will be referred to as the 'ring–long-bar junction'. The knee-piece attachment also has two long bars and a distal cross-bar. The knee-piece may be clamped to the long bars of the splint by means of a screw bolt and hinged plate at the end of each of its long bars.
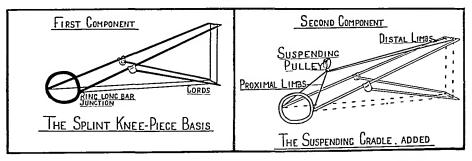
FIG. 365 —Diagram of splint knee-piece basis

FIG 366 —Diagram showing the suspending cradle added

The splint with its knee-piece attached is a familiar method of arranging a fracture so that movement at the knee is possible. In this method this movement is not wanted. The angle which the knee-piece makes with the splint has to be fixed. This is done by the cords. These cords span across, on each side, from the ring–long-bar junctions to the distal cross-bar of the knee-piece and across up to the distal cross-bar of the splint. The distal cross-bar of the knee-piece is thus tied to each end of the splint, and the angle which the knee-piece makes with the splint is thereby fixed.

The splint–knee-piece basis, then, is used as a double inclined plane to which the limb is fixed. The thigh rests in the portion of the splint proximal to the knee-piece and the leg in the knee-piece. When complete the limb lies with the knee flexed at a selected angle fixed by the cords.

2. *Second Component : the Suspending Cradle (Fig.* 366).—This consists of a double pulley and two cords. The cords are fastened to the pulley in such a way that, with the pulley as an apex, the cords radiate as four limbs, delineating a pyramidal space. This pulley will be called the 'suspending pulley'. The pair of cords which run proximally from the suspending pulley to the ring–long-bar junctions will be referred to as the 'proximal limbs'. The other pair running from the pulley to the distal cross-bar of the splint will be referred to as the 'distal limbs'.

When suspended ·by the pulley, the splint–knee-piece basis tends to rotate according to the relative lengths of the limbs. By altering the lengths of these limbs, the suspending pulley at the apex of the cradle is brought farther backwards, distally, proximally, or to one side.

This cradle, then, is the means whereby the fulcrum or point of pivot of the mechanism is regulated. By bringing the suspending pulley proximally, the fulcrum is also brought proximally, and by pulling the pulley nearer to one side the mechanism and with it the 'distal fragment' of the fractured limb is given a rotation to the opposite side.
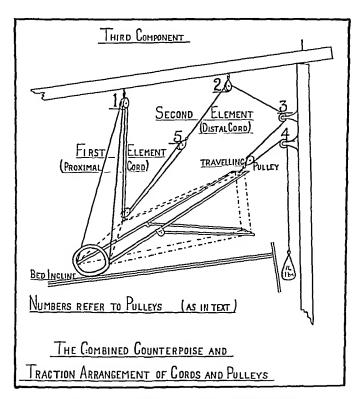
FIG. 367.—Diagram showing the complete apparatus.

3. *Third Component : the Combined Counterpoise and Traction Arrangements of Cords and Pulleys (Fig. 367)*.—This consists of a 'Balkan frame', pulleys, and cords.

Frame.—The frame is the usual familiar article of hospital equipment, which provides a horizontal overhead beam and a vertical distal beam.

Pulleys.—To the overhead beam at distances less than the length of the splint are fixed two pulleys : a double one proximally and a single one distally. These will be called 'No. 1 pulley' and 'No. 2 pulley', respectively. To the vertical beam are fixed two pulleys, one above the other at a height about 2 ft. above the bed. These will be called 'No. 3 pulley' and 'No. 4 pulley' respectively. The positions of these pulleys in actual cases are shown in *Table I*. Their final positions

are fixed when the final adjustments are made. Another single pulley described as the 'travelling pulley' is attached to the distal cross-bar of the splint. An extra pulley is used between the cords to give a compensating sliding attachment. This is termed 'No. 5 pulley'.

Cords.—These comprise two elements, as shown diagrammatically in *Fig.* 367. The first element, or proximal cord, runs from each ring–long-bar junction, up over the double pulley No. 1, back through the double suspending pulley of the cradle, and half-way up to the single pulley No. 2. By the sliding attachment of pulley No. 5, the second element continues the line of the first element up through No. 2 pulley. This second element then continues down around No. 3 pulley, across around the travelling pulley on the splint, back around No. 4 pulley, and so to the weight. The sliding attachment between the two elements is obtained by fastening the second element to the eye of pulley No. 5. This pulley runs in the bight of the first element. The weight used is one of about 10 to 12 lb. and will be referred to as 'the weight'.

The part of this component from No. 3 pulley to the weight is mainly concerned with pulling the mechanism distally. Here the travelling pulley is used to give a true mechanical advantage in producing this pull. The rest of this third component acts mainly as a counterpoise or suspension. It produces an upward pull, but it also produces to some extent a distal pull.

In dealing with a fracture two considerations dominate the procedure. These are the factors of counterpoise and extension, and they must be considered distinctly and individually. Certain cases with deformity and shortening will require the maximum extension, whereas others with good anatomical apposition will not require so much. These latter and also those in the end stages of their treatment may require suspension rather than extension.

Therefore to obtain the *maximum extension* No. 1 pulley must be as far down towards the vertical beam as possible without neutralizing the counterpoise or upward pull unduly. Viewed laterally, the projection down of the line between pulley No. 2 and the suspending pulley should pass proximally to the ring–long-bar junction. The 'afferent and efferent' portions of the cord from either side of the travelling pulley to the Nos. 3 and 4 pulleys should be as nearly parallel as possible. (Because the mechanical advantage gained by means of the travelling pulley is equal to the weight multiplied by a constant, minus an amount for friction. This constant is theoretically equal to two, but it will vary indirectly with the angle of these 'afferent and efferent' portions of the cord to one another.)

With the increase in the extension the foot of the bed must be raised, as the patient's own body weight acts as the counter-extension.

Where conversely the *minimum extension* with suspension is required the cords from the splint and its cradle to the overhead beam may be more vertical. And in the extreme degree of almost pure suspension with no appreciable extension, No. 3 pulley may be dispensed with. The cord then passes from No. 2 pulley straight through the travelling pulley to No. 4 pulley and the weight.

Thus variations to suit the desired requirements of individual cases are possible. Further actions of this component will be considered in the detailed description—that is, with the limb in place and the mechanism controlled by the patient.

DETAILED DESCRIPTION OF THE PROCEDURE
OF SETTING UP A FRACTURE

Assembling the Apparatus.—As in the Hodgen principle, the 'distal fragment' has to be fastened to the distal cross-bar of the splint and/or the distal cross-bar of the knee-piece. The hold on the 'distal fragment' may be obtained by adhesive strapping, ice-tong calipers, or other such method which may be in vogue. In this series of cases 35 have been done with adhesive strapping and the other 15 with ice-tong calipers. Using this method, plain strapping applied to the skin produces the minimum of trauma with the maximum of pull, because the pull is obtained indirectly and from numerous sources and different parts of the limb. The strapping may be applied to the whole limb, to the thigh alone, or to the thigh and leg separately. The loop from the thigh turns distal to the knee and above the leg, and is fastened to the cross-bar of the splint. The loop from the leg turns distal to the foot and is fastened to the cross-bar of the knee-piece.

The manœuvres up to this stage may be done with the patient on an emergency splint. After the hold has been secured on the distal fragment the selected Thomas splint with the knee-piece loosely attached is gently worked on to the limb. The knee is flexed as required. Cross-bands of flannel are clipped beneath the limb across the long bars so as to form a trough for the limb to lie in, in the usual manner. Those for the thigh are fastened to the splint and those for the leg round the knee-piece. The ring of the splint is pushed well on to the ischial tuberosity. The knee is slowly flexed to the desired angle, and the knee-piece clamped tight to its proper place on the long bars of the splint.

The cords to complete the splint–knee-piece basis are now fastened in. These are fastened to each ring–long-bar junction and stretched across to the distal cross-bar of the knee-piece, where they are fastened by a clove hitch. These cords are pulled tighter than required and the whole is allowed to rest on the bed while the cords are continued up to be fastened to the distal cross-bar of the splint. These must be pulled tight enough to give a distinct downward bow to the long bars of the splint. Subsequent stretch in the cords will then not jeopardize the rigidity of the splint–knee-piece basis.

The limb now lies in a double inclined plane and has next to be fastened to it. This is done by a cord from 'the hold on the distal fragment' to the distal cross-bar of the splint or the knee-piece, as the case may be. This cord is worked up tight until the ring presses on the ischial tuberosity. Later when the mechanism is working, the distal pull or extension relieves the pressure from the tuberosity.

The suspending cradle is next attached. The suspending pulley is brought over a spot proximal to the point of balance. The proximal limbs will be shorter the more proximal the site of fracture. The reason for this is explained later on. The case examples in the table of measurements illustrate average settings. The limbs are, at this stage, only fastened temporarily, as most of the later adjustment is to be done with them.

The third component is now arranged. This will vary, as stated, to suit the requirements relative to suspension and extension.

The foot of the bed is then put up on blocks. As *Table I* shows, with a weight of 12 lb. and a setting to produce an average amount of extension, a patient of about 150 lb. weight needs the foot of the bed raised at least 10 in.

Nos. 1 and 2 pulleys are fixed to the overhead beam at distances respectively of about 40 and 24 in. proximal to the vertical beam. Nos. 3 and 4 pulleys are set so that the cross-bar of the knee-piece swings well clear of the bed under all conditions. This is of great importance. The whole effect of the counterpoise is neutralized if any part of the mechanism other than the ring rests on the bed.

The travelling pulley is next fastened to the cross-bar of the splint. The cords of the third component are now threaded in. The cord of the first element is fastened to the inner ring–long-bar junction and its other end is threaded in turn through the inner side of pulley No. 1, the inner side of the suspending pulley, through pulley No. 5, and back through the outer side of the suspending pulley and the outer side of pulley No. 1, to finish at the outer ring–long-bar junction. This latter end is finally fastened after all the other adjustments have been made. One end of the second element is now fastened to the eye of No. 5 pulley, and the other end is passed in turn as has been described through the remaining pulleys to the weight.

Adjusting the Apparatus. Consideration of the Mechanics.—The mechanics must be understood in order to make the adjustments. This entails a little digression.

The portions of the limb proximal and distal to the fracture will be referred to as the ' proximal ' and ' distal ' fragments. The ultimate objective is to suspend the mechanism so that it behaves as a first-class lever—that is, there must be a fulcrum or neutral point about which the mechanism rotates, a proximal arm and a distal arm. As the site of fracture and the fulcrum are made to coincide as nearly as possible, reference to the ' proximal arm ' and ' distal arm ' will imply the portions of the mechanism in relation to the respective proximal and distal fragments.

Considering the suspending or counterpoise element alone : When the proximal arm moves up the distal arm moves down. With the patient lying relaxed in the supine position the weight of the thigh keeps the ring of the splint on to the bed. When the patient raises his buttocks from the bed the mechanism must tip up so that the ring will follow the thigh without lag or undue pressure in any direction. (Discrepancy between the movements of the ring and thigh means, of course, that there is movement between the ends of the fragments.)

The weight of the distal arm imparts a downward rotation. Some pull is thereby given to the cord of the second element. This in turn imparts an upward lift to the suspending pulley. Now this suspending pulley is also a type of travelling pulley. Another mechanical advantage, therefore, increases the pull transferred to the apex of the suspending cradle. Thus the weight of the distal arm, by a mechanical advantage gained at the suspending pulley, helps to produce at the ring–long-bar junction an increased upward pull on the proximal arm. The lighter distal arm can thus be made to counterbalance the heavier proximal one. The excursion of the distal arm will naturally have to be greater than the proximal one. This, then, is a mechanism which the patient can control by a force applied only at the proximal or ring end.

Considering the whole mechanism with the distal traction or extension element added : The distal end is, as it were, anchored by the force applying extension. This force acts through the medium of the travelling pulley. This ' anchoring ' force can be analysed into a horizontal and a vertical element (Nos. 3 and 4 pulleys

are higher than the travelling pulley). The latter vertical element of the force tends to lift the distal up or prevent it from depressing. This tends to disturb the movements of the system we have just considered. It tends to convert the lever into a beam supported at two places. The mechanism, however, will again behave as a lever when only this vertical element is neutralized. This is done by moving the suspending pulley proximally. In other words, a tendency must be established for the moments which depress the distal arm to preponderate. This tendency neutralizes the vertical element of the 'anchoring' force. Thus by merely shortening the proximal limbs there is no longer the same 'anchoring' effect. The movements of the mechanism are again those of a counterbalanced lever. The patient is able to tip the mechanism in the same way as before the force applying extension through the travelling pulley was added. The distal arm moves up and down to correspond with the movements in the opposite direction of the proximal arm, the difference now being that the whole fulcrum appears to travel up farther and its site is less definite. An important point is that the movement of the distal arm will be easier, the greater the distance between the Nos. 3 and 4 pulleys.

Actual Adjustments.—The adjustments are made with the co-operation of the patient. It is essential that all his movements should be painless and free. Settings for two positions are effected. These positions are :—

No. 1 Position.—Supine with buttocks and ring of the splint on the bed.

No. 2 Position.—With buttocks raised, as for the insertion of a bed-pan.

The patient moves himself into these positions with the aid of a 'monkey chain' fixed over the head of the bed. The mechanism is viewed from the side. As the proximal end moves up, the distal end should depress. The point at which the mechanism appears to rotate should be about the site of fracture. If this point is too far distal, the ring of the splint will lag behind the thigh as the No. 2 position is assumed. The correction will be to shorten the proximal limbs of the cradle—that is, to bring the suspending pulley proximally. The opposite fault, causing the ring to press in posteriorly, is unusual. The suspending pulley is then too proximal.

With fractures above the upper third of the femur the suspending pulley may be as far proximal as possible and yet the ring may lag behind the thigh. The further correction then will be to bring No. 1 pulley proximally.

With fractures proximal to the ring, such as the central dislocation of the hip, movement at the fracture cannot be obviated. The best procedure then is to minimize the effort required to produce movement, while the hip-joint may be kept fixed. The neutral point in these cases is best placed just proximal to the knee.

When a fracture is below the knee the distal fragment is fastened to the knee-piece. The travelling pulley is also fastened to the distal cross-bar of the knee-piece, which comes to lie more horizontal. Flexion at the hip-joint is increased. The proximal limbs of the cradle will be longer than the distal limbs (*see Table I*).

Extra flannel bands may now be placed around the limb so as to correct wrong angulations or rotations. These with the cross-bands forming the trough are now finally adjusted and fastened with large safety-pins. Attention is paid to the 'master band' which preserves the anterior bow of the femur.

The limb and the splint may be next wrapped round with a bandage. This bandage is taken up to and woven across the front part of the ring of the splint. Any further alteration to the third component may now be done. Any gross alteration of this component may entail a corresponding alteration to the second component. Finally, the cord comprising the first element of the third component is adjusted and fastened so that the No. 5 pulley is mid-way between the No. 2 and the suspending pulleys.

The patient now performs all his movements, pulls himself to the top of the bed, and by externally rotating at his hip he may roll over to the unaffected side. The bedclothes are tucked around and over the mechanism so that only the cords to the Balkan frame emerge from the covers. This depresses the mechanism very little. The distal end of the knee-piece may have attached the usual foot-piece which holds the foot at a right angle. The distal end is inspected to see that the cross-bar of the knee-piece does not touch the bed. Should this bar even come near to the bed in the No. 2 position, the correction will be to lower the foot of the bed, raise one or both the Nos. 3 and 4 pulleys, or to increase the weight. Should the excursion of the distal end not be sufficient, the correction will be to separate the Nos. 3 and 4 pulleys, having made certain that the suspending pulley is as far proximal as is feasible.

After a day or so the pull distally on the mechanism relieves the tuberosity of the ischium of the pressure of the ring. Should this become exaggerated and the ring pull away by more than two finger-breadths, the cord holding the distal fragment to the cross-bar must be shortened.

The attachments of the knee-piece to the splint take the stress and strain of the whole mechanism. They are crucial points. It is essential that they grip absolutely tightly to their positions on the splint. Later with shrinkage of tissues, pulling out of shortening, correction of deformity and so on, further adjustments such as tightening or replacing bands and readjustments to the strapping may become necessary.

Much later, when union is established, suspension rather than extension may be required. This is provided for by the alteration already described, up to the extent of eliminating No. 3 pulley.

FOUR TYPICAL CASES ILLUSTRATING FOUR DIFFERENT TYPES OF FRACTURE

For comparative purposes as well as for conciseness the weights, dimensions, angles, and other data concerning these four cases have been condensed in the form of a table (*Table I*).

Case 1.—Fracture of the middle third of the femur.

A. T., aged 29. Weight estimated at about 140 lb. Admitted on May 29, 1934, with a fracture of the left femur and other wounds. Adhesive strapping was applied and the limb fixed to the splint–knee-piece basis, while the patient was recovering from his shock. Later he was transported on this basis to the theatre and back. The rest of the counterpoise traction mechanism was completed when the man was returned to bed. He was not X-rayed prior to being put up.

From the beginning he was able to move himself around without any discomfort. As there was no shortening to be overcome there were no further adjustments to be made to

the cord from the strapping to the cross-bar of the splint. On the sixth day the antero-posterior and lateral X-rays were taken (*Figs.* 368, 389). These are as shown. Next day the photographs of the man in the No. 1 and No. 2 positions were taken (*Figs.* 370, 371). After the seventh week the patient left hospital in a weight-bearing caliper, and by the sixteenth week he was able to take weight directly on the limb, and he reported back in the twentieth week walking normally without a limp.

FIG. 368.—*Case* 1. Antero-posterior X-ray photograph after treatment.

FIG. 369.—*Case* 1. Lateral X-ray photograph after treatment.
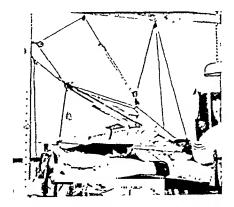
FIG. 370.—*Case* 1. Photograph showing patient in the No. 1 position.
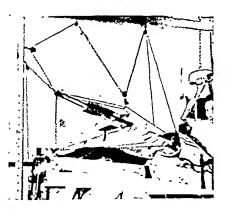
FIG. 371.—*Case* 1. Photograph showing patien in the No. 2 position.

Case 2.—**Fracture of the lower third of the femur.**

W. I., aged 55. Weight 165 lb. before accident. Admitted on June 23, 1934, with a fracture of the right femur. There were numerous abrasions on the leg, and the knee was

FIG. 372.—*Case* 2. X-ray photograph, almost antero-posterior, before treatment.

FIG. 373.—*Case* 2. X-ray photograph, lateral, before treatment.

distended with blood. He was treated by a method of fixed traction, pending the attention of his Benefit Society doctor, for two weeks. X-ray photographs were taken on June 25. These show the case 'before treatment' (*Figs.* 372, 373).

On July 4 the case was officially handed over as a hospital patient. The old strapping was removed. There were numerous sores on the leg. There was about 2½ in. of shortening. Ice-tong calipers were inserted into the femoral condyles and the limb was put up in the counterpoise traction mechanism. Daily readjustments were made to keep pace with the correction of the shortening. On July 11 the condition was stationary, and X-rays and
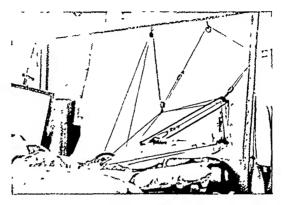
FIG 374.—*Case* 2. During treatment. Note the use of the ice-tong calipers.

FIG. 375.—*Case* 2. X-ray photograph, antero-posterior, after treatment.

FIG. 376.—*Case* 2. X-ray photograph, lateral, after treatment.

photographs were then taken (*Figs.* 374–376). By Aug. 14 the splint–knee-piece basis had been altered so that the patient's knee had been moved to an almost completely extended position. On Nov. 27 the man was walking normally and could flex his knee through 170°–100°.

Case 3. **Fracture of the upper third of the femur.**

W. W., aged 30. Weight about 160 lb. Attended on April 5, 1932, at the Nursing Home, Springs, Transvaal. The fracture was then three weeks old. As much as 30 lb. weight had been applied by direct extension at some time. There was still 2 in. of shortening. On April 5 the limb was put up in the counterpoise traction system. Strapping extension was used. On April 10 the cord to the distal cross-bar of the splint had been shortened by 1¾ in. The patient meanwhile permitted fairly extensive daily manipulations. By Oct. 1 the man was back at his work as a miner. He then had a good alinement with about ½ in. of shortening.

Case 4. **Fracture of the middle third of the leg.**

J. F., aged 19. Weight about 120 lb. Admitted on Oct. 20, 1934, with a compound fracture of the leg. He was cleaned up and put up in a split plaster soon after admission. On Oct. 23 the leg was transferred to a Thomas splint as the wound required frequent dressings. On Oct. 26 the fracture was in very poor position, as can be seen from *Fig.* 377. On Oct. 27 the limb was put up in the *counterpoise traction system*. Ice-tong calipers were

inserted into the malleoli. The travelling pulley was fastened to the distal cross-bar of the knee-piece. The patient was X-rayed again on Oct. 29. This X-ray shows that there was nearly ½ in. of separation between the fragments (*Figs.* 378, 379). This is particularly interesting as the weight used was only 5 lb. No. 2 pulley was accordingly shifted proximally 12 in. and the cord from the distal cross-bar of the knee-piece to the caliper lengthened by ½ an in. The boy left hospital in a plaster on Nov. 17.

FIG. 377.
Case 4. X-ray photograph before treatment.

FIG. 378.
Case 4 Lateral X-ray photograph after treatment.

FIG. 379.
Case 4. Antero-posterior X-ray photograph after treatment.

In *Table I* the data concerning the splint–knee-piece basis, the suspending cradle, and the non-variable factors of the third component are grouped together. These do not vary with the change in position of the patient. These are the factors which can be altered to produce an alteration in the setting of the fracture. The remaining factors grouped under the heading of the ' variable factors ' change with the positions assumed by the patient, but no alteration of the setting of the fracture can occur. In the third case the angles and, by means of spring balances, the tensions in the various segments of cord have been measured and plotted. From the readings parallelograms of forces were constructed to represent the magnitude and direction of the forces acting, when the patient was in the No. 1 and the No. 2 positions. Without knowing the weight of the limb it was possible to calculate the turning moments of the mechanism. The final resultant of the forces could be shown to be exerting a pull distally in the axis of the fractured bone for both the positions.

In practice, however, this mathematical result is obtained by merely altering the adjustments provided until the patient says that movements are painless and that he feels quite safe and rigid and is being pulled strongly down towards the vertical beam of the Balkan frame. One patient said, " It feels as though I am being hung up by the leg ". He felt most of the pull at the posterior part of the calf. The extension on the mechanism may by pressing on the calf hold the leg forward. A flannel band to counteract this is placed over the *front* of the distal third of the leg. This is an example of the production of an indirect pull on the femur exerted through the ligaments of the knee-joint. This pull will vary directly with the angle of the knee-piece to the splint. (Compare the angles in *Cases* 1 and 2.)

Table I.—DATA CONCERNING FOUR CASES OF FRACTURE OF THE LOWER LIMB

Case Numbers	1	2	3	4
1st Component—				
Length of splint	39·3 in.	40·0 in.	39·6 in.	39·3 in.
Length of knee-piece ..	24·5 in.	24·0 in.	24·0 in.	24·0 in.
Angle of knee-piece to splint	42·4 °	28·0 °	39·0 °	36·0 °
Angle of lower cords to splint	26·8 °	17·2 °	22·5 °	21·8 °
Angle of vertical cords to splint	67·8 °	77·3 °	76·0 °	76·5 °
2nd Component—				
Proximal Cords—				
Average of lengths ..	18·5 in.	18·0 in.	9·9 in.	32·6 in.
Inclination to splint ..	23·2 °	20·6 °	31·2 °	14·7 °
Distal Cords—				
Average of lengths ..	23·4 in.	24·0 in.	31·4 in.	11·2 in.
Inclination to splint ..	17·3 °	15·2 °	9·4 °	46·3 °
3rd Component. Non-variable Factors—				
Weights used	10 lb.	12 lb.	12 lb.	5 lb.
Inclinations of beds (to horizontal)	6·0 °	7·3 °	7·3 °	5·0 °
Distance proximal from vertical beam of—				
No. 1 pulley.. ..	38·3 in.	40·5 in.	38·5 in.	39·5 in.
No. 2 pulley.. ..	15·5 in.	25·0 in.	24·0 in.	22·0 in.
Height up from distal surface of bed of—				
No. 3 pulley.. ..	33·5 in.	31·0 in.	33·6 in.	27·4 in.
No. 4 pulley.. ..	27·0 in.	27·7 in.	26·3 in.	18·0 in.

3rd Component. Variable Factors—	1		2		3		4	
Position numbers ..	1	2	1	2	1	2	1	2
Height buttocks lifted from bed	0 in.	5 in.	0 in.	4 in.	0 in.	3 in.	0 in.	5 in.
Inclinations of splint (to horizontal) ..	36·3 °	23·6 °	30·5 °	22·0 °	30·1 °	25·3 °	36·2 °	25·9 °
LENGTHS AND INCLINATIONS OF LINES BETWEEN—								
Ring–long-bar junction and No. 1 pulley—								
Length	38·3 in.	33·8 in.	36·3 in.	33·2 in.	39·4 in.	37·1 in.	41·2 in.	37·4 in.
Inclination	88·5 °	82·4 °	77·1 °	76·0 °	76·8 °	75·5 °	76·5 °	71·6 °
No. 1 pulley and the suspending pulley—								
Length	22·2 in.	20·2 in.	20·0 in.	19·0 in.	28·6 in.	26·6 in.	16·9 in.	17·8 in.
Inclination	67·3 °	65·6 °	80·2 °	73·7 °	97·8 °	96·7 °	51·3 °	45·6 °
Suspending pulley and No. 2 pulley								
Length	25·8 in.	24·2 in.	25·0 in.	23·2 in.	35·0 in.	33·0 in.	15·2 in.	13·6 in.
Inclination	56·8 °	53·6 °	61·5 °	64·7 °	58·5 °	57·8 °	62·9 °	69·8 °
No. 3 and the travelling pulley								
Length	11·8 in.	14·0 in.	16·6 in.	17·1 in.	18·2 in.	17·8 in.	20·1 in.	22·7 in.
Inclination	58·9 °	70·2 °	44·0 °	53·0 °	51·3 °	55·0 °	60·8 °	60·6 °
Travelling pulley and No. 4 pulley								
Length	7·2 in.	8·5 in.	14·5 in.	14·6 in.	13·3 in.	12·5 in.	12·8 in.	15·2 in.
Inclination	29·3 °	51·0 °	34·7 °	45·1 °	31·3 °	34·5 °	39·5 °	43·0 °

The technique used with the calipers and the adhesive strapping may be epitomized thus :—

Calipers.—The application of this implement is treated as a surgical operation in the theatre. Wounds are first attended to, dressed, and bandaged. The surgeon then cleans himself afresh, and likewise the sites for the insertion of the calipers, and a fresh set of instruments is used. The caliper after insertion is well packed round with sterile dressings and a plentiful supply of sterile cotton-wool. A sterile bandage is woven between the tongs of the caliper until the whole is enclosed in dressings, with only the end for the attachment of the cord uncovered. The subsequent removal of any other dressings must not disturb in any way the dressings around the calipers.

Adhesive Strapping.—The salient features here are : Collars of padding are stitched into place over the bony prominences, e.g., the femoral condyles or malleoli. Main straps are placed in the usual manner along the sides of the limb, forming a loop distally. These straps may be taken well above the site of fracture. Their ends are ribboned for about one foot or so. Short narrow strips are then applied so as to cover in spica fashion the main ones, the limb finally being almost encased in a mould of adhesive strapping. The ribboned ends of the main straps are turned back and incorporated with the short spica strips. The whole is next covered with a well-fitting puttee of flannel, stitched into place. The usual rectangular ' spacer ' piece of wood is fitted into the loop of the main straps. The position of this spacer is determined after a few ' trial-and-error ' pulls after the whole has been completed. The cord which fastens the distal fragment to the distal cross-bar of the splint is fixed to this rectangular block of wood and threaded through the loop of the main straps.

CONCLUSION

A method of treating fractures of the lower limb is described. It is particularly intended for fractures of the femur from the upper third distally and for fractures of the upper half of the leg.

The main features are the great amount of ease, comfort, and relaxation experienced by the patient, and the fine degrees of adaptability, regulation, and control which can be effected and maintained.

The method has been used for both hospital and country patients who had to be treated in their homes. The upkeep and after-care is minimal. In the 50 cases so far treated by this method, anatomical replacement has been good in all but 2 cases. Fractures with 2 in. of shortening have been pulled out in a few days. The average time taken completely to assemble and adjust the mechanism has been just under an hour. Subsequent adjustments were all performed in a few minutes. The house surgeons who have been shown how to use the method have had no difficulties, and their results have been good. .

Finally, no intricate or unusual apparatus is required. Operative measures and anæsthetics have been seldom called for. Plain strapping applied to the skin has given the maximum of pull with a minimum of trauma, because the pull is obtained indirectly and from numerous sources and from different parts of the limb.

I would like to thank Professor Brebner for his kindly criticism and for the opportunities he has given me to try this method on the patients admitted under his care; Mr. F. P. Fouche, who taught me the technique and niceties of the Hodgen principle applied to the Thomas splint; Professor Gordon Grant for his valuable criticism and advice concerning the presentation of this paper; Messrs. Moller and Mackenzie, Honorary Surgeons to the Germiston Hospital, on whose patients the method was evolved. I am greatly indebted to Professor Dart and Drs. Galloway and Gillman, of the Anatomy Department, for their enthusiasm, editorial advice, and photographic activities, without which this paper would not have been written. I am also indebted to Mr. Kay and Mr. Mason and Miss Tomkins for their help with the photographs and X-rays.

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RENAL RICKETS AND DWARFISM: A PITUITARY DISEASE

By BRUCE CHOWN

CHILDREN'S HOSPITAL OF WINNIPEG, AND GRACE HOSPITAL, IN ASSOCIATION WITH THE
MEDICAL COLLEGE OF THE UNIVERSITY OF MANITOBA

IN the past two years I have seen two babies, sisters, having from birth deformities like those of severe rickets. A few days after birth they began to have curious spells of sham joy. Both had a hypercalcæmia but normal or slightly reduced phosphatæmia without discernible progressive decalcification of the skeleton. One died at three months and the other at six. Both had early pathological changes in the kidneys, which would have led to chronic nephritis. At first I thought that these were cases of congenital osteitis fibrosa cystica, but now believe that the two children were suffering from a form of the disease variously called ' renal rickets ', ' dwarfism ', or ' infantilism '. If this is true, then the cases add weight to the opinion that these diseases are due to endocrines running amok, the kidneys being but innocent bystanders.

CASE REPORTS

Family History.—The parents, Mr. and Mrs. L., are first cousins of English-Welsh extraction. There are no dwarfs or giants in the family so far as is known. Mr. L. has been married twice. His first wife, pregnant but once, bore him a son, and died four years later of some acute febrile illness. The son has a boy of four years. These two, the son and grandson, are apparently normal. Mr. L. was 33 years old, Mrs. L. 20 years, when they were married in 1916. The record of Mrs. L.'s pregnancies is as follows :—

1	2	3	4	5	6	7	8	9
E+O	●	●	●	♂	♂	♀	GWEN	JEAN

E+O = Ectopic and removal of blood cyst of ovary

● = Miscarriage. 5 and 6 were stillborn. 8 and 9 are the cases here reported

In the first two years after her marriage her teeth " went chalky " and were pulled. She weighed 115 lb. in 1916, 183 lb. in 1927, and now weighs 159 lb. She is an active, bright, intelligent woman of 38, normal on physical examination; blood Wassermann repeatedly negative; basal metabolic rate —12; calcium and phosphorus balance normal; X-ray pictures of skull, pelvis, arms, and legs normal. Her menses began when she was 15 and have been regular. She has always suffered from severe premenstrual occipital headaches. When she is pregnant she feels particularly well; never suffers from nausea, vomiting, salivation, sweating, or excessive dryness of the skin; her hair grows long and thick, only to fall again after childbirth. Mr. L. is a rather small 52-year-old normal man of 125 lb.; blood Wassermann negative. Their 6-year-old girl is normal.

Case 1.—Gwen (C.H. No. 32–3039). In this pregnancy Mrs. L. was admitted to hospital at the seventh month and again at the eighth with false labour pains. The baby, however, was born at term after a four-hour labour; weight 7 lb. Deformities, although undoubtedly present, were not noted at birth. At 10 days she began to have convulsions, for which she was admitted to the Children's Hospital at 3 weeks. She weighed 6½ lb.; temperature 101° to 102°, then normal; pulse 114 to 140. There were present a maculo-papular eruption over her legs and feet, slight internal strabismus, pliable cranial bones such as one often finds in a newborn premature infant, beading of the ribs, enlargement of wrists, anterior angulation of both tibiæ (*Fig.* 380). An area of skin 3 × 4 mm. over either point of angulation was hairless, smooth, and adherent to the tibia; in comparable areas over each fibula was a small pit overlying an exostosis, while over the posterior aspect of the right ulna was a small hairless area neither adherent nor depressed. Owing to a short metacarpal bone the right middle finger was the same length as the fore and ring fingers. The left second toe crossed over the third. The lymph nodes and liver were not enlarged; the spleen and kidneys not palpable. The knee-jerks were hyperactive; Chvostek's and Trousseau's signs absent. There was a moderate polymorphonuclear leucocytosis. The spinal fluid was said to contain 59 cells per c.mm., 70 per cent polynuclears, but I think this doubtful. The Wassermann reaction was negative in
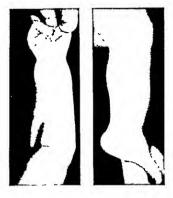
FIG. 380.—*Case* 1. Showing enlarged wrist and angulated tibia.

both blood and spinal fluid. X-ray examination showed widespread bony lesions (*Fig.* 381), which were then interpreted as probably syphilitic. After four days' observation the child was sent home on bottle feedings and antisyphilitic treatment. She had only one minor convulsion in hospital.
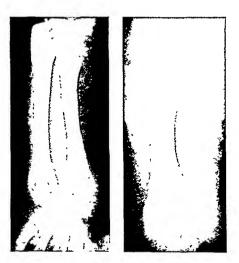
FIG. 381.—*Case* 1. X-ray at 3 weeks of femur, radius, and ulna, showing marked rachitoid cupping.

At home she took her artificial feedings eagerly, and, though she vomited, her mother thought she was doing well. Then one night five weeks after discharge she uttered loud cries. These were repeated the following night, while on the next day " she cried out like an idiot and threw her arms and legs around or would contract her whole body." (This type of spell was observed in detail in her sister and will be described in a separate paper.) She was re-admitted to hospital the next day. She now weighed 6 lb.; temperature 101° to 104°, then down to normal with an occasional rise to 101°; head 13¾ in., chest 12¾ in., abdomen 11 in., against a normal 14½ in. for each of these. The baby's general condition was unchanged from her previous admission. Once more the spinal fluid was reported to contain an increased number of cells. In the blood there was a marked polymorphonuclear leucocytosis—36,700, with a slight anæmia—3,800,000. The urine twice contained a trace of albumin and once a few pus cells. The blood calcium was 15·5 and 15·8 mgrm. per 100 c.c., the phosphorus 5·4. She took her milk badly, vomited much, gained about 2 oz. a week. At times her colour was grey; she cried out, moved her head from side to side, or waved her hands as though distressed After two and a half weeks in hospital her temperature rose suddenly to 104°; she was cyanosed, almost continually on the move, cried out. In two days her temperature was down to 101° but there was no other clinical improvement. She vomited blood. Three days later she was dead.

Case 2.—Jean (C.H. No. 34–8391).   During this pregnancy Mrs. L. took calcium and viosterol.   She was admitted to Grace Hospital at the eighth month with false labour pains, but again carried to term, being delivered of a 7 lb. 6 oz. girl after a two-hour labour.   The baby, like her sister, began on the 10th day having convulsive seizures, which appeared to be controlled by calcium.   She was sent home and given calcium and viosterol, but these were soon stopped, since it seemed probable that they might lead to calcification of soft tissues.   Through the generous co-operation of Drs. F. A. Benner and H. Medovy, I saw the baby when she was 5 weeks old.   Her blood calcium was 17 mgrm., and her phosphorus 4·8 mgrm. per 100 c.c., her mother's 10 5 and 2·1.   She continued well, though without any gain in weight, till she was 7 weeks old.   Seizures then recurring, she was admitted to Grace Hospital under the care of Drs. Benner and Medovy, and a week later was transferred to the Children's Hospital for investigation.

She now weighed 7 lb. ; temperature 100° F ; head 14¼ in., chest 12¼ in., abdomen 13½ in., length 21½ in.   She was well proportioned ; eyes round ; skin soft and dry ; cranial bones widely separated (?) ; marked beading of ribs ; liver edge 1 in. below the costal margin ; both kidneys palpable at the level of the navel, and hard ; spleen not palpable ; wrists and ankles not enlarged.   X-ray examination showed widespread bone lesions (*Fig.* 382).   Her nervous manifestations will be considered separately.   She took her feedings very slowly ; was extremely constipated ; lost 4 oz. the first week, and looked dehydrated.   In view of this and the fact that dehydration sometimes takes place in hyperparathyroidism, she was at Dr. Medovy's suggestion, given extra water by stomach tube.   The result was astonishing.   She gained 10 oz. in four days and her fever fell to 100°.   But, though water was continued, the fever again rose, and up to the time of her death she had recurrent bouts.   A general view of her subsequent course may be gathered from *Fig.* 383.   Certain special features will be dealt with separately.

FIG. 382.—*Case 2.*   Antero-posterior and lateral X-ray views of femur, tibia, and fibula. While the anterior view of the femur suggests a lesion somewhat like that in *Case 1*, the remaining ones are suggestive of cyst formation, but the rarefactions represent osteoid.   This picture was constant from first observation at 5 weeks to death at 6 months.

Autopsies.—Both bodies were examined after death.   Although carefully searched for I found only two minute parathyroid glands in each case.   There certainly was no parathyroid tumour or hyperplasia in either.   Serial sections of the pituitary in the first case were not obtained.   The available sections are histologically normal.   In the second, serial sections proved the presence of hemi-agenesis of the partes posterior et intermedia (*Fig.* 383).   Histologically the gland was otherwise normal.   The thyroids, too, were histologically normal, but the second had small bilateral accessory lobes
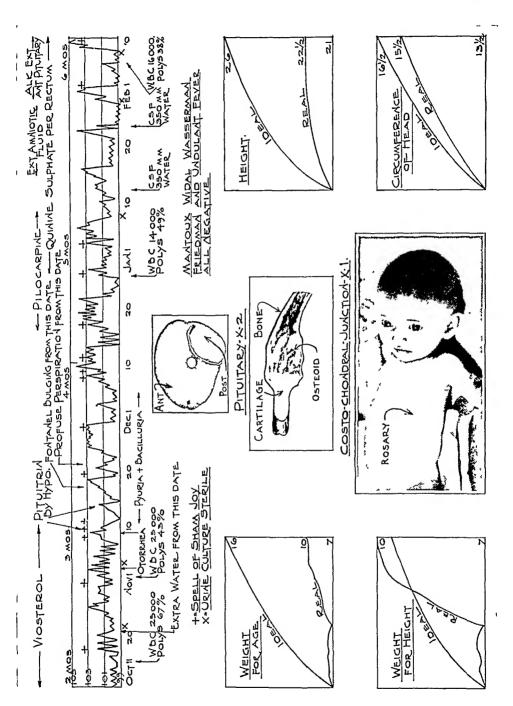
sticking forward from the edge of the lateral lobes like blinders on a horse's head. The thymus in the first case was small; in the second it weighed 7 grm. Microscopically the cortex and medulla were clearly differentiated, the corpuscles very small and pale with scarcely any eosinophil substance. The ovaries and adrenals in both were normal. In the brain and spinal cord of the first patient no pathological lesion was found. The brain of the second was not externally diseased, but histological investigation is not yet completed. The heart, lungs, liver, pancreas, gastro-intestinal tract, ureters, and bladders in each case were normal. The bones, kidneys, and pituitary were diseased.*

Bones and Growth.—We have not sufficient data relevant to the first patient *to say definitely that she was a dwarf. All we can say is that, in spite of* adequate feedings, she failed to gain weight. The second patient, although of average size at birth, became a dwarf, yet there was not complete absence of growth, but an interesting differential growth-rate (*see Fig.* 383). It would appear that this actually killed the child, for, the skull growing more slowly than the brain, there was an ever increasing intracranial pressure, with final respiratory paralysis. This in itself is curious. In an infant with progressive hydrocephalus skull growth keeps pace with the size of the expanding brain, even though bone growth may not quite keep up with it. But here there appeared to be inability of bone to grow and of the bones of the cranial vault to separate, for at autopsy it was found that the margins of the bones of the vault were really in apposition, a broad edging of osteoid having given, during life, the semblance of wide separation of the sutures. In six months she grew approximately $1\frac{1}{4}$ in. (32 mm.), or $\frac{3}{8}$ in. (19 mm.) in the four months of observation in the Children's Hospital, but growth was of cartilage and osteoid, not bone, as shown by the following figures :—

	SEPT. 14, 1934	JAN. 10, 1935	GROWTH
Length of shadow—diaphysis of femur	74 mm.	74 mm.	0
Length of shadow—diaphysis of tibia ..	67 mm.	67 mm.	0
Distal end of femoral diaphysis to proximal margin of epiphysial ossification centre	3 mm.	7 mm.	4 mm.
Distal end of femoral diaphysis to proximal end of tibial diaphysis ..	28 mm.	35 mm.	7 mm.

At autopsy, while the degree of lesion varied in different bones, there was a similar type in all. The shafts of the long bones were of normal hardness, but the metaphyses were so soft that the bones easily bent at these points. The lesions were most marked at the lower end of the femur and at costo-chondral junctions

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* The horizontal section of the pituitary shown in *Fig.* 383 is the result of a reconstruction from serial sagittal sections. It can be seen that a sagittal section taken through the centre of the gland, or to the right of centre, would appear normal, and also that absence of posterior lobe in a section to the left might carelessly be passed as due to post-mortem technique. The bulging back of the left half of the anterior lobe made the gland outline so slightly irregular that, though I was looking particularly for a lesion of the pituitary, I did not realize one was present until all the serial sections had been examined. The sections were cut by Miss Service, of the Department of Anatomy of the University, through the kind co-operation of Professor Inkster.

(see Fig. 383). On section there was a greater or less accumulation of osteoid in the metaphyses and at the epiphysial line, irregularity of the epiphysial cartilage, and in some cases a transverse vascular zone between cartilage and bone. There were no cysts.

Histologically there was : (1) Delayed senescence of cartilage, so that (*a*) long tongues of uncalcified cartilage extended into the osteoid, and (*b*) small islands, both calcified and uncalcified, persisted within trabeculæ at some distance within the shaft; (2) Failure of the zone of preliminary calcification to form; (3) An enormous overproduction of osteoid ; (4) Some focal increase, in the osteoid area, of osteoclasts without fibrosis. The condition is not identical with avitaminotic rickets since there is no great increase in the depth of proliferating cartilage, while there is a tendency to the formation of islands and peninsulas of cartilage. This difference has been noted before in renal rickets, the best microphotograph that I know of being that of Vogt's[1] patient 1.

Mineral Metabolism.—The following observations were made :—

Name	Age	Date	Ca	P	Remarks
Gwen ..	2 months	16/7/32	15·5		
		19/7/32	15·8	5·4	Died 4/8/32
Mrs. L.	36 years	18/1/33	9·9	2·7	
	38 years	14/9/34	10·5	2·1	Not nursing
Jean ..	5 weeks	14/9/34	17·0	4·8	
		10/10/34	14·9		After convulsion
		13/10/34	18·0	3·9	
		19/10/34	15·4	3·0	After convulsion
	3 months	29/10/34	15·3	3·4	
		5/11/34	15·0	3·3	
	4 months	26/11/34	14·3	3·5	Urea nitrogen 12·4
	5 months	3/1/35	17·5	4·0	
		14/1/35	16·7		C.S.F. Ca. 7·6
	6 months	29/1/35	18·4		C.S.F. Ca. 5.5

DAILY BALANCE

Mrs. L., Oct. 1934				Jean, Nov. 1934		
Intake	Output	Balance		Intake	Output	Balance
2·09	1·64	+ 0·45	Calcium	0·72	0·40	+ 0·32
	S. 1·29				S. 0·35	
	U. 0·35				U. 0·05	
3·29	3·29	+ 0·005	Phosphorus	0·59	0·36	+ 0·23
	S. 1·08				S. 0·18	
	U. 2·21				U. 0·18	

S = Stool   U = Urine

Urinary Tract.—A trace of albumin was present in each specimen of Gwen's urine and a few leucocytes in one.   In all of Jean's there was a trace of albumin, a specific gravity of 1005 to 1010.   Four cultures at monthly intervals were sterile, though there were usually from one to eight cells per high-power field in the uncentrifuged urine.   In her third month *B. coli* was grown from the urine, and for a short time in her fourth month, when clinically she was better than usual, the urine contained *B. fæcalis alkaligenes* and 20 to 30 cells per high-power field At this time the cells were mainly pus cells, but at other times there were also large and small round cells and giant cells 30 μ in diameter with a single round nucleus. At times coarsely granular casts varying in size and number were found in fresh specimens, but not, as a rule, in routine samples collected one night and examined next morning.   On the following grounds these were considered to be a calcium salt in an undetermined matrix : (1) The upper part of the centrifuged urine contained less calcium than the lower, e.g., 12·03 as compared with 16·37 mgrm. per 100 c.c.; (2) They stained black with silver nitrate in the light ; (3) They stained red with alizarin ; (4) They disappeared when suspended in urine of P_H 4·8 ; (5) They persisted when suspended in urine of P_H 8·0 ; (6) When they were acidified with weak acetic acid under the microscope the granules disappeared, leaving transparent rods like slightly crumpled cellophane.

Neither baby was thirsty or voided large quantities of urine.   During her fourth month Jean's blood-urea nitrogen was 12·4 mgrm. per 100 c.c.

In both babies the kidneys reached to the umbilical plane and felt hard and lobulated.   No special note was made of the state of the ureters and bladder in Gwen's case, and post mortem the kidneys appeared normal in the gross.   Jean's bladder was not dilated according to X-ray examination, while both it and the ureters were normal post mortem.   Her kidneys were pale, hard on section, and weighed together 69 grm., against the normal of 51 grm. for her age or 40 grm. for her weight.

Microscopically* (*Fig.* 384) the same types of lesions were found in both cases,

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* Since the lymphatics are not recognized as playing a part in the physiology of kidney function, my interpretation of the abnormal deposits in these kidneys as being calcium in lymphatics is open to question.   There can be no question of their presence.   Part stains black when treated with silver nitrate in the light, part red with alizarin, part has the microscopic configuration of calcium carbonate, and part takes a bluish-purple stain with hæmatoxylin.   All this suggests a complicated substance of protein-calcium-phosphate-carbonate nature or a mixture of substances.   Further they do not lie in the tubules but in juxtaposition to them, often surrounding a tubule like a collar of beads.   In shape they vary from round to long oval   About some a membrane with flattened nuclei can be seen.   These circumscribed calcium-salt deposits must derive their elements eventually from the bloodstream.   They may either be directly deposited from the blood into these peritubular spaces, or else filtered from blood-stream to glomerulus to tubule, then passed back through tubular epithelium into these same spaces.   There seems no reason why the first should take place The second process is much more consonant with modern physiological theory even though it diverges from that theory in introducing the lymphatics, as intermediaries for some substances at least, between tubule and vein.   In the present cases the excessive amount of calcium in the blood leads to an abnormal amount in the glomerular fluid   Part of the excess calcium in the primary urinary filtrate is passed back into the lymphatics.   Calcium differs from most re-absorbed substances in readily forming an insoluble salt.   Thus it has done here, the precipitate remaining as evidence of what has been going on.   What part the lymphatics play in the normal physiology of the kidney is not known.   In preliminary work, in association with Miss Margaret Lee and Mr. John Teal, lesions similar to those here described have been readily produced in young rats by injections of parathormone.   A further study of renal calcinosclerosis is in progress and will be reported later.
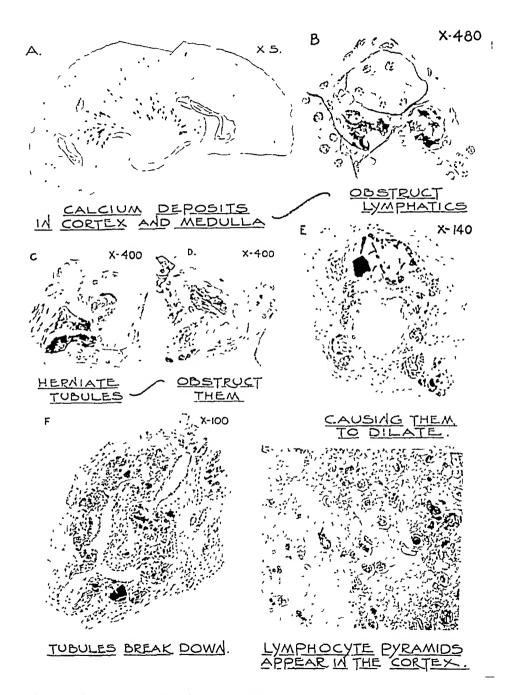
FIG. 384.—Early stages in the evolution of the kidney lesion. (Owing to the reduction of the illustration, the magnifications shown should be approximately halved.)

but they were more advanced in the second.   In lymphatics accompanying tubules there were deposits of calcium salts alone or with a hæmatoxylin-staining material. As the deposits became larger they pushed in the wall of the tubule, obstructing it and breaking it down.   There was low-grade inflammation, the tubules draining inflammatory cells, albumin, and débris.   Minute pyramids of round-cell infiltration appeared in the cortex.   The glomeruli, blood-vessels, and pelves remained essentially normal.

DISCUSSION

We may assume the two babies suffered from the same disease.   They had from before birth malformation of the partes intermedia et posterior of the pituitary. At birth they were of normal size but had deformities like those of severe rickets. After birth they failed to grow at the average rate, or in other words became dwarfs. They had many nervous manifestations referable to diencephalo-pituitary imbalance. They had hypercalcæmia, calcium casts in the urine, calcium deposits in the renal lymphatics, focal necroses in the kidneys, and the elder one so-called pyelonephritis. I believe the calcareous fragments in the kidneys of these two babies may be the Rosetta Stone of renal rickets, leading not only to a true interpretation of this disease, but also to an explanation of certain other renal ruins.

The concept of renal rickets is of very recent origin, for while Lucas[2] in 1883 recorded the association of albuminuria with rickets in adolescents, it was not until Fletcher[3] showed a case before the Section for Diseases of Children of the Royal Society of Medicine in 1911 that interest was aroused.   Later an occasional adolescent with acutely developing genu valgum died suddenly in uræmia following osteotomy.   Post mortem there were found rickets-like lesions of the metaphyses, most marked as a rule at the lower ends of the femora, together with strangely distorted, gnarled kidneys.   Barber,[4] in a series of papers, gave excellent descriptions of the disease and emphasized polyuria as a presenting symptom, whereas Ellis and Evans[5] stressed moderate dilatation of the urinary tract.   Gradually there emerged a picture of rickety deformities occurring in infancy or at puberty, or occasionally after an acute illness, the patients later dying of renal failure.   Some were dwarfs and some sexually infantile.   Often there was a history, which might go back for years, of great thirst and of the passage of copious quantities of urine of low specific gravity, containing a trace of albumin.   In some cases there was a pyuria.   There might be hypertension, sometimes with arteriosclerosis.   Always there occurred the gnarled kidneys and the leather-tipped bones.   There could be no doubt the two were in some way causally related, and, since rickets ordinarily is not recognized as producing any kidney disease, the reverse relationship was considered probably the true one :   the chronic nephritis caused the rickets. Shipley[6] and his co-workers suggested a chemical explanation of the disease which Parsons[7] developed :   the kidneys could not excrete phosphate, so the gut did ; there the phosphate united with the calcium, preventing the latter's absorption and so causing a " low calcium rickets."   Parsons further showed that there were at least two types of the disease, or two diseases which appeared the same but were probably different.   Teall[8] confirmed this from an X-ray standpoint.   The dwarfing was looked upon as due also to the chronic nephritis, being likened to the dwarfing of congenital heart disease.

There was, as Hunter[9] and others have pointed out, much against the explanation of the disease being symptomatic of renal failure. It is impossible to extend the chemical theory to the fœtus so as to account for congenital deformities. Ordinary chronic nephritis is not, either in adult or child, associated with rickets even when there is phosphate retention; where rickets and chronic nephritis are associated the latter is always of a peculiar type. Nephritis has never been proved to produce dwarfing, much less infantilism. The urinary tract dilatation remains an unexplained observation.

Albright, Baird, Cope, and Bloomberg[10] have suggested that the disease in some cases may be really an infantile form of hyperparathyroidism. They cite Parsons's[7] case who had a hypercalcæmia, and their case, K.S. This girl of 13 had had a diagnosis of renal rickets made previously, but on the basis of hypercalcæmia an exploration was carried out, a single parathyroid tumour found and removed. The calcium now fell, the phosphorus rose, and the girl developed chronic tetany and cataracts. Functionally she had only one parathyroid. Radiologically she showed a bone lesion very similar to that in patients with renal rickets, whereas, as the authors point out, other children with hyperparathyroidism have not shown this X-ray picture.

Hutinel[11] reported a girl who at 3 years suffered for fourteen days from headache and vomiting; at 8½ years she was treated for genu valgum; polyuria and polydipsia developed; at 11 years she had albuminuria and œdema. When seen at 13 she had rachitic bone changes, the urine was abundant and contained albumin, and renal function was impaired. He believed the dystrophy was caused by alteration of the glands of internal secretion and particularly the hypophysis (Mitchell's[12] summary).

I believe that Hutinel's interpretation of his case was the correct one and, as Harris[13] suggested, renal rickets is primarily a pituitary malfunction, which may, like any pituitary disease, have certain polyglandular variants. Such an explanation fits well with observed facts, which are difficult to explain on the basis of primary chronic nephritis: the polyuria, the dwarfing, the infantilism, the urinary tract dilatation. The first three are well recognized as pituitary-diencephalic in origin; a word as to the fourth. The bladder and ureters receive both sympathetic and parasympathetic fibres. Without entering into the controversy as to the rôles either section of the autonomic plays in urinary tract contraction and relaxation, I think one may state the following as facts. Dilatation of the bladder sometimes occurs following injury to the spinal cord (sacral autonomic fibres) and may be relieved by resection of the presacral nerve[11] (thoraco-lumbar outflow). Relaxation or contraction of the kidney pelvis, ureters, and bladder can be brought about at will by drugs acting on the autonomic nervous system.[15] Sympathetic and parasympathetic centres exist in the diencephalon.[16] " The diencephalo-hypophyseal can only be properly interpreted when looked upon as a whole." (Cushing). Therefore a worn or ill-made part in this mechanism might produce not only diabetes insipidus (diencephalon), dwarfing (growth-promoting factor of the anterior pituitary), infantilism (sex-stimulating factor of the anterior pituitary), but also urinary tract dilatation (diencephalon). This may sound very theoretical, but in the second case here reported there was such an ill-made part associated with dwarfing and congenital rickets. Langmead and Orr's[17] patient with renal infantilism and late rickets had a malformed pituitary and hyperplasia of the parathyroids.

The nephritis can be explained as the result of calcuria and phosphaturia. In the presence of an increased excretion of these minerals part is passed out in the urine, but part is re-absorbed through the tubular epithelium to the peritubular lymphatics. Here, whether from concentration, change in reaction, or what not, calcium is precipitated as the insoluble calcium phosphate and carbonate. The deposits obstruct first the lymphatics and then, by pressure, the tubules. Some tubules and their glomeruli atrophy from complete obstruction. Some dilate from partial obstruction. In some areas comparable to those shown in *Fig.* 384 F the epithelium grows back again, but there remain sacculations or so-called cysts.[18] The ill-drained and badly damaged kidney becomes a *locus minoris resistentiæ*. Wave after wave of acute interstitial nephritis (pyelitis[19]) comes and goes, leaving destruction in its wake, but also dissolving some of the tell-tale stony fragments. At last the kidney 'fails'. Phosphates are no longer excreted. Calcium and phosphorus are diverted more and more to the gut. Depletion begins. Both physiological and pathological sources are drawn upon. The deposits in the kidneys disappear, and when the child dies of uræmia there remain only the dwarfed and misshapen corpses of the kidneys. It may be that I am wrong in trying to wash the mineral deposits out of these failing kidneys. They quite possibly persist, but, occurring in association with fibrosis, have been looked upon as an end-result of the sclerosing process and so not mentioned. Thus Mitchell[12] only says of his case, R.P., " There was fibrous change in the interstitial tissue of the kidney ", yet the microphotograph appears to show calcium in this interstitial tissue (? lymphatics).

The drama of hyperparathyroidism has so fixed its characters in the medical mind that every calcuria cloaks a parathyroid villain, and " *Cherchez la hyper-calcæmie !* " is the watchword of every detecting laboratory. A false syllogism has been set up. " All hypercalcæmics have calcuria. Patients with renal rickets have no hypercalcæmia. Therefore patients with renal rickets have no calcuria." The major premiss is true but not exclusive. Calcuria does occur in the presence of hypercalcæmia, but it may also occur in its absence. Thus in Cushing's[16] Case 15 of pituitary basophilism with a blood calcium of 9·8, Aub, who studied the patient metabolically, found " the calcium output [in the urine] was far in excess of normal ". A normal calcium figure for the blood does not prove that the kidneys are not being attacked under this flag of peace. It is to be recalled, too, that in renal failure the blood-calcium level falls and the phosphorus rises, so that a hypercalcæmia may be camouflaged in this way. Further, in renal (pituitary) rickets it is not necessary to think of the process as continuous. The calcuria may only appear at the springing-up periods, and indeed a case such as Langmead and Orr's[17] can only be explained on the assumption of a noxious agent acting intermittently. Their patient was first seen at 14 with retarded growth and development and chronic nephritis but no rickets. Six years later he rapidly developed genu valgum and died of renal failure. The chemical theorist would explain this as a chronic nephritis which first retarded body growth, and only later, when renal failure had reached the stage of phosphate retention, caused demineralization and rickets. It would be hard to gainsay such a possibility, were it not that this very case showed at autopsy a malformation of the pituitary and enlargement of the parathyroids. The endocrinophil may here visualize the pituitary spring flood of infancy carrying down silt to clog the kidneys ; then a long drought, with stunted growth, the dry period extending far past its wonted time ; at last the torrential

pituitary rains of adolescence, washing deep gulleys in the hills and sweeping the débris down to complete the destruction of the kidneys.

But there are a few cases on record of renal rickets which had a hypercalcæmia at one time or another. Karelitz and Kolomoyeff[20] observed a child from the age of 4½ to 6 years. When she was first seen her blood calcium was 10·6, her phosphorus 8·0, and her urea-nitrogen 143. She was given viosterol. The calcium rose to 11·0, phosphorus dropped to 4·2, and urea-nitrogen to 73. According to X-ray examination her bone lesions improved. Viosterol was stopped. Calcium continued to rise to 12·4, phosphorus held at 4·4, and urea-nitrogen fell to 54. Viosterol was started again, to be shortly replaced by cod-liver oil. In six months the calcium was 9·4, phosphorus 7·8, and urea-nitrogen 171. The disease progressed to death six months later. Before death calcification of blood-vessels and lymph nodes was made out, which had not been observed five months before, whereas the bone lesions had advanced with remarkable rapidity. In Duken's[21] patient in uræmia, when viosterol was given, the bones healed, calcium rose from 10 to 16, phosphorus fell from 8 to 6, and non-protein nitrogen from 107 to 30. In Parsons's[7] patient, H.T., who had a blood calcium of from 10 to 14·6, phosphorus of 4·1 to 10·07, and a urea of 112·9 to 136·5, the above relationship did not hold, the calcium, phosphorus, and urea rising and falling together. This patient, Parsons thought, was made worse by ultra-violet radiation. Incidentally Teall reported the X-ray picture of the skull in this case as "identical with that of Paget's disease". Lightwood's[22] delightfully reported "Case of Dwarfism and Calcinosis" had a blood calcium of only 11·0 but a phosphorus of 6·68 and urea of 169 a few days before death, yet the fibrotic kidneys contained deposits of calcium in tubules and in glomerular remnants. The parathyroids were reported as definitely not enlarged, but the pituitary was not mentioned. I think the 11·0 mgrm. of calcium per 100 c.c. in the presence of renal failure must here be interpreted as a masked hypercalcæmia, and that this case was a variant of pituitary rickets. In Karelitz and Kolomoyeff's patient there appeared to be first an improvement and then a rapid progress in the disease. Their case, it seems to me, can be interpreted somewhat as follows : Calcinosis of the kidney, the result of pituitary rickets, had gone on to beginning failure. Viosterol caused at first withdrawal of minerals from soft tissues, including kidneys, to bone (X-ray evidence). The kidneys, relieved of the mineral obstruction, improved in function, with consequent rise in calcium and drop in phosphorus and urea. The continued use of vitamin D produced the reverse effect, the bones lost calcium, the soft tissues, including the kidneys, took it up, renal function fell rapidly, and the child died in uræmia.*

Such a result has been reported in experimental hypervitaminosis D.[23] There is an analogous parallel for this reversal of action in work emanating from Collip's

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* The orthodox teaching at the moment is that vitamin D controls absorption or excretion of calcium through the intestinal wall. In massive doses, however, it produces decalcification of bone, and in continued small doses increased calcification, i.e., a systemic effect. The above case suggests a sensitivity to vitamin D, just as Parsons thought his patient was made worse by ultra-violet light, so that an ordinarily physiological dose produced the effects of massive doses. Wilder, Higgins, and Sheard[25] have suggested that the parathyroids determine sensitivity to vitamin D, sensitivity to the vitamin increasing in parallel with activity of the gland. Ham and Lewis[26] have produced in rats a lesion indistinguishable from rickets by the exhibition of ergosterol.

laboratory, Selye[24] having shown that whereas parathormone first caused decalci-fication of bone, continuation of the extract produced hypercalcification. Smyth and Goldman[27] recorded a remarkable case of a boy who developed rickets and enormous deposits of calcium phosphate following a streptococcal septicæmia. He died of renal failure. At autopsy the parathyroids were enlarged, while during life his blood calcium had run around 12 mgrm. and his phosphorus from 12 to 16 mgrm. The pituitary was not remarkable in the gross. This case, like Hutinel's,[11] may, I think, best be looked upon as a counterpart of Simmonds's disease, an injury to or functional depression of the pituitary causing in one case an upset in mineral metabolism, in the other in fat metabolism. Smyth and Goldman were of the opinion that the enlargement of the parathyroids in their patient was a secondary phenomenon.

This brings us back to the possible relationship of the parathyroids. In the case of baby Jean the small calcium output and good retention were surprising. There was also a good phosphorus retention, but the normal partition of stool 2 to urine 1 has been changed to a 1 to 1 relationship. This latter taken with the blood chemical findings is suggestive of hyperparathyroidism. The pituitary probably has a parathyrotropic function.[28, 29] Collip[30] has brought evidence to show that any particular hormonal level of activity depends upon a balance between a hormone and its anti-hormone. In the present case the chemical findings of hyperpara-thyroidism could be brought into agreement with the histological evidence of normal parathyroids by assuming the absence of the parathyroid anti-hormone. One would have to go farther and assume that since there was mal-development of the pituitary the latter was the governor of anti-parathyroid hormonal activity. I must admit, however, that I do not find the position a happy one. On the other hand, it is to be noted that histologically there is no evidence of osteoclastic release of calcium, the osteoclasts occurring among osteoid trabeculæ. The hypercalcæmia can be ascribed simply to normal absorption with failure of deposition. The parathyroids might then become drowsy owing to the sedative action of the calcium, so that one could conceivably have a hypoparathyroid state in the presence of a hypercalcæmia.

Up to this point, then, evidence and argument have been brought to show that the minor symptoms of renal rickets may best be accounted for as due to pituitary mal-function, and the nephritis to a calcuria or phosphaturia, which in turn is the result of faulty bone metabolism. The argument must finally turn on the relationship of the pituitary to the bone lesion, and here proof fails. Bone metabolism is affected by mineral intake, vitamins, inflammation, trauma, the parathyroids, the gonads, the thyroid, and the pituitary. The lesion in question simulates or actually is rickets, which in turn can be produced experimentally by avitaminosis D, by hypervitaminosis D,[26] by thyroidectomy,[31] by parathyroidec-tomy.[32] Rickets, ordinary avitaminotic rickets, is in some way related to growth, for if growth ceases the rickets will heal,[13] and is also related to sex, for it is more common and more severe in males.[33] Renal rickets, too, manifests itself at what Harris[13] calls " the springing-up periods ", the times of rapid (pituitary) growth. But, curiously, growth does not take place ; there is preparation for growth but failure of the bones to add to their length. There is tubulation without elongation. This suggests that there are normally two factors active in bone growth and that here one has failed. As fast as bone grows at the epiphysis it is remodelled at the

metaphysis. At puberty, in health, these two processes speed up *pari passu*. Suppose them governed by the pituitary through two of its subsidiaries, then if it were at fault it might speed up the process of metaphysial resorption (perhaps via parathyroids) without building new bone (perhaps via thyroid). Osteoid would be thrown out to buttress the weakened bone. The minerals made available by resorption would be excreted by the kidney. Renal calcinosis would develop. The picture is complete. This speculation is best closed by again quoting Harvey Cushing : " Of all subjects that engage the attention of the profession at the present day, that of endocrinology particularly lends itself to the temptation of impressionistic speculation." Amen.

The argument in proof of the thesis that a lesion of the pituitary-diencephalic mechanism is the primary cause of the symptom complex called renal rickets is, then, as follows : (1) Malformation of the pituitary has been found in these cases ; (2) The associated symptoms of dwarfing, polyuria, infantilism, and urinary tract dilatation can be caused by such a lesion ; (3) The nephritis is not primary but is secondary to an abnormal mineral metabolism, itself the result of faulty bone growth ; (4) The faulty bone-growth therefore not being due to the nephritis, and the remaining symptoms being due to pituitary-diencephalic disease, it is to be presumed that the bone disease is due to the same cause. Should this argument prove correct, it offers some hope for these previously hopeless cases, for substitution therapy could in theory produce normal bone growth in the springing-up periods and so save the kidneys from being stoned to death.

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ISOLATED DISLOCATION OF THE BASE
OF THE FIFTH METACARPAL

By NORMAN ROBERTS

ASSISTANT ORTHOPÆDIC SURGEON, LIVERPOOL ROYAL INFIRMARY

AND C. THURSTAN HOLLAND

CONSULTING RADIOLOGIST, LIVERPOOL ROYAL INFIRMARY

CARPO-METACARPAL dislocations of the thumb are relatively frequent, and in combination with a Bennett fracture through the base of the metacarpal constitute a common injury. Isolated dislocations of the second, third, and fourth metacarpal bones have been reported on numerous occasions, but a careful search of the literature reveals only one previously reported case of isolated dislocation of the fifth metacarpal on the carpus. McWhorter,[1] who reported this case in 1918, had been unable to find any record of a previous case.

In addition to isolated dislocations of individual metacarpals, multiple dislocations occur, and simultaneous dislocation of all five metacarpal bones has been described (Burk[2]). In a review of the literature, Burk quotes twelve cases of dislocation of the base of the fifth metacarpal in association with other dislocations. In seven cases it was dislocated dorsally, completely in each case, and in five cases anteriorly, two being incomplete.

Speed[3] states that no case of isolated dislocation of the fifth metacarpal has been recorded, and other text-books on fractures omit reference to the condition or state that it is unknown. Stimson[4] does not mention the condition.

The writers have been able to collect radiographs of four cases and the clinical details are available in all but one.

Case 1. (C. T. H.'s case).—This patient, a man aged 53, in getting off a bus fell heavily on his left side with his left hand between his body and the roadway. He noticed that his little finger looked to be "out of place", and went to his doctor, who "put it straight". Five days after the injury the whole hand was considerably swollen, the fingers stiff, and bruising was present over the inner metacarpal region. A fracture of one of the inner metacarpals was suspected.

The radiographs (*Fig.* 385) show a complete dislocation of the base of the fifth metacarpal, the latter being displaced inwards and forwards with consequent shortening of the finger.

Attempts at reduction failed entirely, and radiographs taken later on showed the condition to be unchanged. Five months after the accident there was almost complete functional recovery, his doctor estimating it as a 95 per cent good result.

Case 2.—The details and radiographs of this case have been obtained by one of us (C. T. H.) through the kindness of Dr. Sankey, of Oxford. The patient, an adult male, injured his hand in March, 1931, and was found to have dislocated his fifth metacarpal. The radiograph (*Fig.* 386) shows an inward dislocation of

the fifth metacarpal with shortening of the finger, the base of the metacarpal lying immediately to the ulnar side of the unciform.

Attempts to reduce the dislocation failed, but when he was re-examined in September, 1933, he was found to have excellent function. The grip on the inner side of the hand was slightly impaired but there were no painful symptoms. The patient was following his normal employment as a bus cleaner and had not lost a day's work in consequence of the injury.
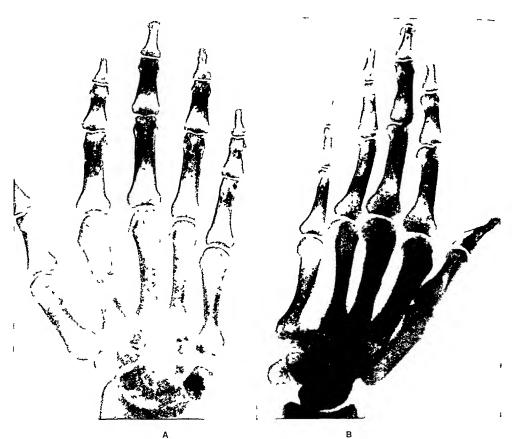
FIG 385—*Case* 1   Dislocation of fifth metacarpal bone · A, Hand, palm down,
B, Semi-lateral view.

Case 3. (N. R.'s case).—The patient, a woman aged 31, slipped and fell on the left hand on Jan. 21, 1935. The diagnosis was not made on clinical examination, but when the radiographs (*Fig.* 387) had been taken the patient was re-examined more carefully and was found to have definite shortening of the finger with a painful and unduly prominent base of the fifth metacarpal.

Reduction was easily accomplished by traction on the finger combined with local pressure over the metacarpal and no anæsthetic was necessary since the finger was relatively painless. On releasing the traction the dislocation immediately recurred. The finger was splinted on a wire frame splint with traction on the finger obtained by skin extension, and in this position the dislocation remained reduced

completely. Traction was maintained for three weeks and then discontinued under the impression that the reduction was stable. However, when the patient was re-examined on June 28, redisplacement had occurred, but not to the extent of the original displacement. The functional result was excellent, the only abnormality being a tendency for the finger to drift into a position of ulnar abduction when the hand was relaxed. Full active adduction of the finger was possible.

Case 4.—In this case, from the late Dr. Robert Knox's collection, no clinical details are available beyond the fact that the patient was an adult male. The illustration (*Fig.* 388) is one of a pair of stereoscopic radiographs which show that

FIG. 386.—*Case* 2. Dislocation of fifth metacarpal bone : hand palm down.

the proximal end of the bone was lying in front of the bases of the third and fourth metacarpals.

The first three cases are almost identical, the base of the metacarpal being displaced inwards and forwards. Reduction of the displacement is easily accomplished, but unless continuous traction is exerted the dislocation recurs. This is accounted for by the fact that the articulation relies for its stability entirely on its ligamentous connections. In order to maintain a stable reduction it would probably be necessary to continue immobilization with traction for four to six weeks.

The fourth case is matched by McWhorter's case, the only other previously reported. His patient, a man aged 23, sustained a dislocation of the fifth metacarpal
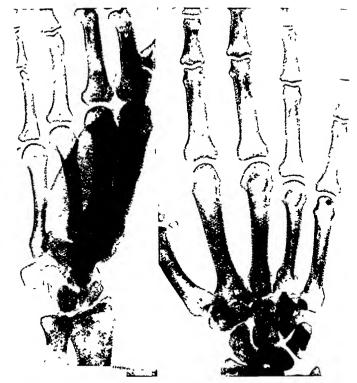
FIG. 387.—*Case* 3.   Dislocation of fifth metacarpal bone : similar displacement to *Cases* 1 and 2.

FIG. 388.—*Case* 4.   Proximal end of fifth metacarpal dislocated forward into palm of hand.

two weeks before he was admitted to hospital. Radiographs showed a marked forward and outward displacement of the base of the fifth metacarpal. This case is evidently an exact parallel to the fourth case in the present series. Attempts at manipulation failed entirely to alter the position of the displaced metacarpal and consequently open operation was undertaken. An extensive dissection of the palm was necessary to free the bone, but it was successfully replaced and remained stably reduced. Good functional recovery occurred in a few weeks.

It seems probable that in cases of this type with extreme displacement of the base of the metacarpal across the palm a closed reduction would be difficult or impossible. Open operation may therefore be resorted to, although it appears to be entirely unnecessary in the other cases in which the displacement is to the inner side and is less extreme.

SUMMARY

1. Four cases of isolated dislocations of the base of the fifth metacarpal are described. One other case has been previously recorded.

2. Two types of displacement are exemplified by the present series ; one an extreme degree of outward displacement and the other a less extreme inward and forward displacement.

3. Reduction of the latter group should be easy, but a long period of continuous traction is necessary to maintain the corrected position.

4. Open operation may be necessary for those cases in which the metacarpal is displaced outwards across the palm.

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RUPTURE OF THE LONG HEAD OF THE BICEPS BRACHIALIS

WITH NOTES ON FOUR CASES

By H. A. H. HARRIS

ASSISTANT SURGEON AND ORTHOPÆDIC SURGEON, CHELMSFORD HOSPITAL

THE four cases of rupture of the long head of the biceps which form the subject of this paper were all seen between June, 1934, and February, 1935. Nevertheless it is an uncommon injury. Thus Harry Platt,[1] writing in 1931 on ruptures of tendons generally, said that he had never seen a case. In 1925 Gilcreest,[2] in an exhaustive paper, pointed out that little had been written on the subject in English but that there were several lengthy papers in the French and German literature. Loos[3] in 1900 had collected 62 published cases, to which he added 11 more. By 1927 McKenna[4] found 81 cases in the literature, including those of Loos, and he himself added 1 more. He pointed out that of the 81 cases, only 15 had come to operation. Rankin[5] in 1933 described 4 further cases. It would appear, therefore, that fewer than 100 cases have so far been published and that hitherto no writer in this country has recorded his experience of the condition.

Etiology.—In the writer's four cases the patients were all men, their ages varying between 51 and 92, and in each case the right arm was involved. The patients were all lean, wiry subjects with arteriosclerotic changes in the peripheral blood-vessels. In one the Kahn reaction was strongly positive, and in this case the rupture occurred from direct injury to the biceps, although the violence was not applied at the point of rupture; in another case the injury occurred in a motor accident and the mechanism of its production could not be ascertained. In the two remaining cases indirect violence was the cause. It is probable that there is always an osteo-arthritis of the shoulder and that this is a predisposing cause of the condition.

Diagnosis.—Rupture of the long head of the biceps produces a characteristic syndrome, and the diagnosis should never be difficult. The patient complains of a sudden acute pain in the upper limb, usually in the region of the shoulder-joint, and he notices thereafter that the arm is weak. The pain is aggravated on voluntary flexion of the elbow, and supination of the forearm is also painful. On telling the patient to flex the elbow, one finds that the lateral half of the belly of the biceps contracts into a firm circumscribed mass, about the size of a tangerine orange. This mass is drawn down towards the elbow-joint and one feels an 'emptiness' above it. In the two cases seen within a few days of the accident it was possible to palpate the tendon of the long head lying coiled up in this space and it felt like a worm lying just beneath the skin. If the case is not seen until some months after the injury, this 'coiled worm' sensation is not noted, for the effusion organizes into fibrous tissue which binds the coils of the tendon together and they thus lose their identity. In some cases the coiled tendon is not felt for the reason that the ruptured portion remains in the bicipital groove.

Anatomical Considerations.—In some cases the tendon gives way at its origin from the rim of the glenoid cavity—that is, the injury is a true avulsion. In other cases the rupture occurs at the upper end of the bicipital groove, and here it would appear that a ridge of osteophytes running between the tuberosities of the head of the humerus causes friction which leads to flattening and ' fraying ' of the tendon—that is, the injury is a rupture of the tendon in its continuity. When the rupture takes place at the glenoid rim it sometimes happens that the tendon is not drawn out of the bicipital groove into the arm. If such a case is untreated at the time, the tendon will then take up a new, but unstable, attachment in the groove. This is a most important practical point, for when one comes to explore the biceps at operation the muscle appears to be intact and it may seem, at first sight, and unless one is aware of this contingency, that the diagnosis is in error. In these cases the tendon must be dragged away from its new attachment in order to deliver it into the wound.

Treatment.—To restore full strength and function to the limb it is manifest that the treatment must be operative. To leave so large a portion of the biceps with an absent or unstable attachment must inevitably weaken the arm to an extent that will almost certainly prevent a manual worker from carrying out his former employment. In old people, and those whose occupation is sedentary, operation need not be insisted upon, and this applies particularly to those cases in which a new attachment has been acquired in the bicipital groove.

A restoration of the normal anatomy of the biceps is clearly unattainable when the tendon has been avulsed from its origin. When the rupture has taken place in the bicipital groove, direct suture is equally impracticable, for in these cases the ends of the tendon are frayed and thinned.

The long head of the biceps is, to a certain extent, an abductor of the arm. This, however, is a subsidiary part of its function and may be ignored. The important consideration is to restore its power of flexing the elbow and supinating the forearm. This may be attained by suturing the tendon in such manner that it will reinforce the action of the short head of the muscle.

The writer's friend and teacher, the late W. H. Trethowan, was probably the first to solve the problem. In 1921 he operated upon a case in which the diagnosis of avulsion of the long head of the biceps had not been established beforehand. The injury was of some months' duration and the clinical evidence suggested that the rupture had taken place either in the belly of the muscle or at the junction of the belly with the tendon. Trethowan solved the problem which confronted him in his customary inspired fashion by attaching the ruptured tendon to the coracoid process of the scapula, having first passed it through the origin of the short head. The steps of this operation are as follows :—

A long incision is made, beginning at a point medial to the coracoid process, just below the clavicle. The incision passes laterally for about 3 in., whence it curves downwards, in the long axis of the humerus, to a point 2 or 3 in. above the elbow-joint. The triangular flap of skin thus mapped out is reflected medially and the biceps is now exposed and its condition investigated. If the tendon is not found lying coiled up in the arm, the space between the deltoid and the insertion of the pectoralis major is dissected free and the deltoid is retracted laterally. The tendon of the long head is now exposed, and with a sharp jerk it may be pulled free from the new attachment which it may have acquired in the bicipital

groove.   The coracoid process is next identified lying deeply between the deltoid and the clavicular head of the pectoralis major.   The periosteum over the coracoid is split vertically and elevated, and a small incision is made through the origin of the short head of the biceps.   A long Mayo-Oschner forceps is now thrust from before backwards through this incision, and it is made to pass beneath the insertion of the pectoralis major, and anterior to the teres muscles, so that it emerges in the middle of the arm to the lateral side of the belly of the short head.   The end of the ruptured tendon is seized in the forceps and pulled upwards through the origin of the short head, to the belly of which it will now come to lie parallel and slightly posterior.   The tendon of the long head is sutured to the periosteum of the coracoid process, two or three stitches also being placed to attach it to the origin of the short head, through which it is passing.   Unabsorbable material should be used for the sutures, the writer having a personal preference for silkworm-gut.   Before suturing the tendon in its new position it is essential that it should be pulled as taut as possible, with the elbow flexed and the forearm supinated and lying well in front of the chest.   In this position the new origin and the insertion of the long head are approximated towards one another, and it is attained by fixing the hand of the injured side to the opposite shoulder.   This position is maintained until the removal of the stitches at the end of twelve days.   For the next fortnight a ' collar-and-cuff' bandage is worn, and during this time the patient is encouraged to perform active contractions of the biceps.   After this a sling, with the elbow at a right angle, is worn for a few days, and then full extension of the elbow, in which gravity assists, is gradually allowed and active movements of the shoulder-joint in all directions are encouraged.

Ludington[6] has pointed out that the following alternative methods have been suggested : (1) Suture of the ruptured tendon to the pectoralis major (Hoffmann); (2) Suture in the sulcus intertubercularis (Roloff); (3) Suture to the short head of the biceps (Bazy); (4) Suture to the coracoid process of the scapula (Perthes). Colton and Morrison[7] have recently advocated (5) Looping the torn tendon round the insertion of the deltoid.   The first and fifth methods would clearly yield poor anatomical and functional results, while the second method introduces considerable technical difficulties.   It will be seen that the method the writer has described, which is to be attributed to Trethowan, is a combination of the third and fourth methods.   There is no doubt that it yields excellent results, it is not difficult to perform, and, as one patient has expressed it, his " arm feels quite as strong as it did before the accident "—this statement being borne out by the fact that he is able to crank the engine of a heavy motor lorry which has become stiff through standing all night in cold weather.

CASE REPORTS

Case 1.—A. C., male, aged 51, omnibus overseer.   Referred to the writer on June 21, 1934, by Dr. S. Allman Hall, of Dunmow.   This patient had been cranking a fire-engine a few days before, when the engine back-fired and he experienced sudden sharp pain in the right upper arm and shoulder region.   (" The engine was very tight, and as I came to the top of the swing it back-fired and forced my arm down straight.").   The arm felt very weak and he was unable to use it for anything demanding even moderate strength.   On examination the diagnosis of rupture of the long head of the biceps was quite obvious.   On voluntary flexion of the elbow the lateral part of the belly of the biceps contracted into a firm circumscribed mass, and just above this the tendon could be felt lying coiled up in the characteristic

manner described above. There was little or no discoloration or swelling from effused blood. At operation on June 28 it was evident that the tendon had torn out from its origin at the glenoid rim. The operation described above was carried out and progress was uneventful. Three months later voluntary power in the biceps was normal and the movements of the shoulder- and elbow-joints were complete. The only abnormality to be detected was that on contraction the whole of the belly of the biceps appeared to have been displaced slightly inwards, this appearance being accounted for by the new direction of the muscle fibres.

Case 2.—W. W., male, aged 65, labourer. Referred to the writer by Dr. J. H. Hall, of Maldon. Six weeks previously the patient had been involved in a motor collision. On examination the characteristic signs of rupture of the long head of the biceps were evident. It was not possible to elucidate the precise mechanism of the rupture. This man's general health was not satisfactory—he had extremely tortuous, hard arteries, with a blood-pressure of 246/150, and chronic emphysema. In view of this, and since his work was not heavy and he expressed himself himself as able to do it, operation was considered inadvisable.

Case 3.—E. B., male, aged 60, farm worker. Referred to the writer by Dr. R. C. Little, of Witham. Eight months previously the patient had been lifting a full bucket of milk from beneath a cow with his elbow flexed (i.e., the biceps strongly contracted), when the cow kicked forwards with its hind leg and its hoof struck the middle of the biceps. There was a good deal of discoloration of the skin from effused blood, but the precise nature of the injury was evidently not diagnosed at the time. The arm was rested for four weeks and the man then resumed his occupation. He remained at work for six months, when pain and weakness in the arm compelled him to give up. On clinical examination the lateral half of the belly of the biceps contracted into a firm rounded mass above which the characteristic 'emptiness' was felt, but the tendon was not palpable. At operation the tendon of the long head was seen in its normal position, and it was clear that the ruptured tendon had taken up a new attachment in the bicipital groove. The tendon was jerked away from this adventitious attachment and sutured to the coracoid process in the manner described above.

Case 4.—A. M., male, aged 92, retired Army coach. This patient, an extremely hale and hearty old gentleman, had been a well-known athlete in his younger days, and even at his present great age it is his invariable custom to walk four miles every day in all weathers. The rupture of his biceps was caused by reaching suddenly for something above his head. When seen a few hours later, all the characteristic signs were present, including the 'coiled worm' sensation in the gap above the retracted belly of the long head. In view of his age, operation was not advised.

SUMMARY

1. The literature of rupture of the long head of the biceps is briefly reviewed.

2. The clinical features and etiology of the condition are considered.

3. An operation for the repair of the ruptured tendon, together with its appropriate after-treatment, is described in detail.

4. Notes of four cases of the injury are appended.

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PROGRESSIVE   POST-OPERATIVE   CUTANEOUS GANGRENE

By H. T. COX

RESIDENT SURGICAL OFFICER,
WITHINGTON MUNICIPAL HOSPITAL, MANCHESTER

THE facts herewith recorded relate to a case of progressive post-operative cutaneous gangrene developing in a patient operated on for a perforated duodenal ulcer. This case is presumably the fourth of its kind to be reported in Great Britain.[1]

The patient, a man of 44 years, was admitted to Withington Municipal Hospital on Jan. 8, 1935, with an acute abdominal crisis of nine hours' duration. On examination the symptoms and signs presented were those of an acute perforated peptic ulcer. Immediate laparotomy was performed and the diagnosis confirmed, the ulcer being present on the anterior wall of the first part of the duodenum. This was sutured in the usual way and the fluid in the peritoneal cavity partially evacuated. Closure of the abdominal wall was carried out in layers with the addition of silkworm-gut tension sutures and a small rubber drain in the lower end.

The immediate post-operative period was uneventful. Sepsis, however, became evident on the seventh day as shown by a profuse discharge of pus from the lower end of the wound. The tension sutures were removed on the twelfth day. The localized discharge persisted until the fourteenth day, when wound infection became general. There was pain, tenderness, redness, and induration around the whole extent of the abdominal incision. This generalized inflammation then subsided, leaving a small persistent area at the site of the skin puncture which marked the point of emergence of the upper tension suture, i.e., on the left side of the incision. Inflammation at this point slowly but steadily progressed. A purulent ulcer developed with a narrow black band of gangrene at its margin. On the outer side of this band lay a zone of tender induration with an ill-defined edge; on the inner side there appeared a white slough rapidly assuming a dirty greenish colour.

As the lesion increased in size the central slough became detached in portions, revealing healthy, red, granulating tissue. This unusual lesion therefore presented very definite characteristics. Four zones were readily recognizable: an outer zone of tender induration, bluish in colour, with an ill-defined edge and about 1 in. in width; a second zone of black gangrene, about $\frac{1}{2}$ cm. in width, with sharply demarcated edges, situated at the spreading margin of the ulcer; on the base of the ulcer two more areas, the slough originally white but now of a dirty green colour, and, where this had separated, healthy, red, granulating tissue.

The temperature ran an even course with an occasional short bout of pyrexia up to 100° F. No enlargement of the axillary or inguinal glands was detected. All local therapeutics failed to arrest the spread of infection. The lesion continued

to progress with the maximum area of spread on the left lateral side; its right lateral margin never transgressed the scar of the original incision.

FIG. 389.—Photograph taken three days prior to excision.

FIG. 390.—Drawing of specimen of progressive post-operative cutaneous gangrene after excision.

On Feb. 3, twenty-six days after operation, when the ulcer measured $3\frac{1}{2}$ by $2\frac{1}{2}$ in., a diagnosis of progressive post-operative cutaneous gangrene was made. The ulcer was covered with gauze, sealed with collodion, and widely excised with

a scalpel under intravenous evipan anæsthesia. The tissues removed included the ulcer with 1 in. of surrounding skin on the left lateral side, 1 cm. on the right lateral side, and all subcutaneous tissues down to the aponeurosis. *Fig.* 389 is a photograph of the condition taken three days before excision, and *Fig.* 390 is a drawing of the specimen after excision.

The patient refused a skin-graft, but the wound had completely epithelialized three months after excision.
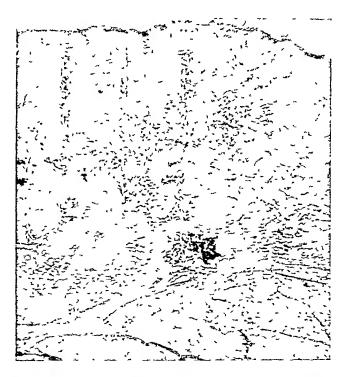
FIG 391 —Section through spreading edge showing limitation of the infection to the epidermis and true skin   (× 15)

PATHOLOGICAL REPORT.—I am indebted to Dr. Dawson for the following pathological reports :—

> *Pus from Ulcer.*—Microscopically and on cultivation. *Streptococcus pyogenes* was present in large numbers.
>
> *Blood-count.*—White blood-cells..   16,100
> Polymorphs   ..   .   .   79 per cent
> Lymphocytes   .   .   .   18   ,,
> Monocytes   .   .   .   3   ,,
> Eosinophils   .   ..   .   —
> Basophils ..   .   .   —
>
> *Wassermann Reaction.*—Negative.
>
> *Pus from Ulcer after Excision* —A non-hæmolytic streptococcus was isolated which grew indifferently under aerobic and strict anaerobic conditions. A heavy growth in peptone broth was inoculated subcutaneously into a guinea-pig and did not cause a general infection or local inflammation.

Section of Ulcer through the Spreading Edge (Fig. 391).—Histological examination showed necrosis of epidermis and dense leucocytic infiltration of the corium with early slough formation. The underlying subcutaneous tissues are relatively uninvolved.

The reasons for presenting this case as an example of progressive post-operative cutaneous gangrene are : (1) The presence of a definite zone of black gangrene ; (2) Microscopic evidence that the spreading margin is limited to the true skin ; (3) The failure of local therapeutics ; and (4) That it occurred after operation.

I wish to express my thanks to Dr. Gamble, Medical Superintendent, and Mr. Holt, Consulting Surgeon, for permission to report this case.

REFERENCES

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INTRAVENOUS PYELOGRAPHY IN A SERIES OF CASES AFTER TRANSPLANTATION OF THE URETERS

By G. GREY TURNER, LONDON
AND JAMES H. SAINT, NEWCASTLE-UPON-TYNE

THE condition of patients in whom the ureters have been transplanted into the sigmoid colon presents two aspects of considerable interest and importance. The first concerns the pathological changes which may take place in the upper urinary tract and their effect upon renal function, and the second, the rôle played by the large bowel in the storage of urine.

Certain clinical observations, pertinent to the first aspect, were made by the senior author in his study of the after-history of a series of 17 personal cases published in this JOURNAL in 1929.[1] They were as follows: "Judged by the standard of the general health, it may be said that none of the patients in this series shows definite evidence of gross renal insufficiency. At the outset I must say I feel convinced that most of these patients develop some degree of ascending renal infection. This is borne out by the fact that in the two cases in which it has been possible to make post-mortem investigations there has been definite and gross evidence of its existence, in spite of the fact that during life neither of these patients suffered from symptoms indicating its presence."

Because several patients of the series were in good health at the time of publication of the paper though they had previously suffered on various occasions from symptoms indicating renal infection, it was further stated that: "From these clinical observations it would appear that a moderate degree of renal infection is not inconsistent with average good health and well-being."

For more exact information regarding pathological changes which may have taken place in the upper urinary tract, we have depended until recent years upon ascending pyelograms, but it would be difficult, as well as highly undesirable, to ascertain in this way information regarding kidneys the ureters of which have been transplanted into the colon. It is natural, therefore, that for use in such cases we should acclaim and hasten to take advantage of the advent of *uroselectan*, the iodine-compound dye which is opaque to X rays and which, after injection into the circulation, is excreted by the kidneys and thus not only serves the same purpose as ascending pyelography but also, by the degree of the density of its shadow, gives some indication of the functional activities of those organs.
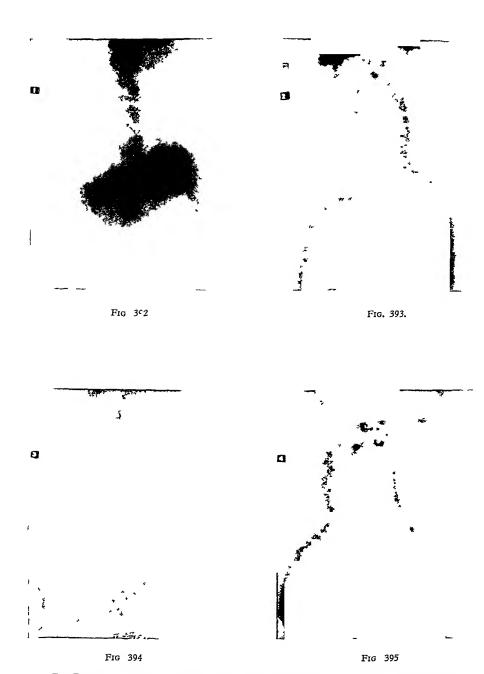
The fact that not only the rectum but the entire colon might act as a reservoir for the urine was mentioned in the publication referred to above, when it was stated: "The problem of where the urine is actually stored in the bowel is of great interest. It cannot be in the rectum, for this part of the bowel is quite unable anatomically to contain the quantity of fluid which sometimes collects. . . . Post-mortem specimens showing enlargement and distension of the colon suggest that the whole of the large bowel may act as the reservoir."

We thought that uroselectan might also be able to contribute to the solution of this problem, for it was felt that the shadow shown by the dye would demonstrate the level to which the urine had risen in the rectum or colon. It was obviously necessary for our purpose, however, that the quantity of urine in the bowel, when taking the X-ray, should be as great in amount as possible, and we therefore decided to allow six hours to elapse after the injection of the dye, no evacuation of the bowels taking place in the meantime.

The investigation was undertaken in six cases, in all of which the operations had been performed by the senior author at the Royal Victoria Infirmary, Newcastle-upon-Tyne, while he was a member of the honorary staff of that institution. Four of them, all subjects of congenital defects of the bladder and urethra, were reported in full by him in the publication to which reference has already been made. They are the first four the results of whose investigations are described below, and the numbers in parentheses are those which they bore when reported on that occasion. The remaining two cases were operated upon at a later date ; in one the condition present was ectopia vesicæ, and in the other vesico-vaginal fistula following injuries during parturition.

All the cases were admitted to hospital for this investigation. The patient was given an ounce of castor oil in the afternoon of the day previous to the investigation and allowed only a light supper. No further food was partaken of until after the completion of the investigation. The bowels were evacuated shortly before 9 a.m., when the dye was injected into the median basilic vein with the usual precautions and technique for such a procedure. Uroselectan B was used, it being the outcome of further research by von Lichtenberg and Binz, the discoverers of uroselectan itself, and possessing three distinct advantages over the original compound in that (1) it is made up in ampoules ready for use, (2) only 20 c.c. need be injected in contrast to the 100 c.c. of uroselectan, and (3) it is much more certain in its results. Once the dye was injected, the taking of fluids was discouraged, for it was felt that they might augment the amount of urine to such an extent as to render necessary evacuation of the bowels before six hours had elapsed and so defeat the object of the second part of the investigation. X-ray films of the abdomen were taken by a portable apparatus at the following intervals after injection : (1) 5 minutes, (2) $\frac{1}{2}$ hour, (3) $1\frac{1}{2}$ hours, and (4) 6 hours.

A brief history of each case is given in the following pages, together with a description of the uroselectan films and the latest available report on the condition of the patient.

FIG 3C2

FIG. 393.

FIG 394

FIG 395

FIGS 392-395 —*Case 1*   Uroselectan films taken 5 minutes, ¼ hour, 1½ hours, and 6 hours respectively after injection of the dye

CASE REPORTS

Case 1 (No. 2).—Mrs. E. S. (*Fig.* 416), aged 41 at time of uroselectan investigation, April 21, 1933.

HISTORY.—Ureters transplanted in November and December, 1914, on account of epispadias with incontinence, the patient then being 22 years of age. Uninterrupted recovery from both operations and has enjoyed very good health since. Married in November, 1916. First child born in 1920 and a second in 1922. Patient about seven months pregnant when admitted for investigation.

UROSELECTAN FILMS (*Figs.* 392–395).—

Fig. 392 : Right—only one (dilated) calix seen.
    Left—normal pelvis and lower calices of kidney are seen. The upper 3 in.
     of the ureter is visible and shows slight dilatation.
    This film was taken at such a level as to cut off the upper poles of the
     kidneys.

Fig. 393 : Right—shadow of kidney plainly visible; all calices show dilatation, this
     being especially well-marked in those of the upper pole. No ureter
     seen.
    Left—kidney shadow has disappeared. About another inch of ureter is seen
     just below that portion on *Fig.* 392 and shows slight dilatation.
    There is a faint shadow in front of the sacrum.

Fig. 394 : Right—the calices are shown much as in *Fig.* 393, but the shadow is of
     slightly greater density. The pelvis of the kidney and the whole of
     the ureter above the brim of the pelvis are visible and are much dilated.
    Left—no kidney shadow seen. The ureter is shown much the same as in
     Fig. 393.
    The density of the shadow in the pelvis has increased to such an extent as
     practically to obliterate the outline of the fœtal head.

Fig. 395 : Right—faint shadow of upper calices and ureter still seen.
    Left—no kidney or ureteric shadow present.
    The shadow in the pelvis is very dense and has extended so as nearly to fill
     it. The iliac, descending, and transverse portions of the colon are not
     outlined, but the dye is present in good concentration in the cæcum
     and ascending colon as far as the hepatic flexure.

The blood-urea was 35 mgrm. per 100 c.c.

SUMMARY OF CONDITION OF KIDNEYS (19½ years after transplantation of both ureters).—On the right side the kidney is the seat of a well-marked hydronephrosis and the ureter is also much dilated. The failure of the dye to give a good shadow in the first film indicates some impairment of the renal excretory function. The obstruction present is of sufficient degree to cause retention of the dye in the kidney and ureter for 6 hours. The left kidney appears normal both as regards structure and function, but the ureter is slightly dilated, indicating that a mild degree of obstruction is present.

LATEST REPORT (April 10, 1935).—The patient states that her general health is good. While the length of time between evacuations of the bowels varies somewhat, the average is about six hours. The longest interval was from 5.30 p.m. to 9.0 a.m. the following morning. Her third child was born on June 24, 1933, about two months after her investigation. The confinement was normal, although she thinks the pain was greater than on the last occasion eleven years previously. The baby was normal and has progressed satisfactorily and the mother made a splendid recovery from the confinement.

FIG 396

FIG. 397.

FIG 398

FIG 399.
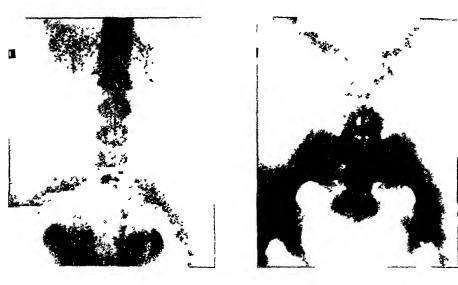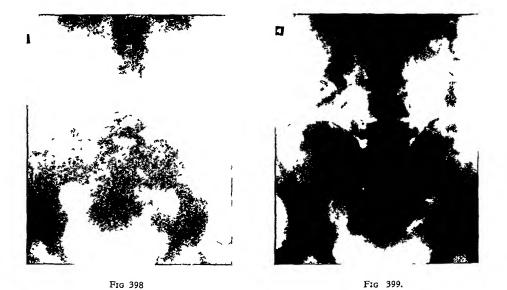
FIGS. 396–399.—*Case* 2   Uroselectan films taken 5 minutes, ½ hour, 1½ hours, and 6 hours respectively after injection of the dye.

Case 2 (No. 5).—V. K. (*Fig.* 417), aged 20 at time of uroselectan investigation, Nov. 30, 1931.

HISTORY.—The ureters were transplanted in August and September, 1917, because of ectopia vesicæ, the patient being then 6 years old. Following the transplantation of the second (right) ureter, her condition began to give rise to anxiety, vomiting, abdominal distension and loss of weight occurring together with a slight evening rise of temperature. The abdominal wound was opened with sinus forceps and about 10 oz. of pus evacuated; two weeks later a further abscess was found in the abdominal incision. Under the anæsthetic a mass was discovered in the right loin; another incision was made close to the iliac crest and a retroperitoneal abscess evacuated. After a short period during which the pulse and temperature were elevated, the patient gradually improved and was soon able to leave hospital. The mucous membrane of the bladder was removed in April, 1921. She has enjoyed excellent health and has developed into a fine, strong, healthy, young woman. An X-ray of the urinary tract taken before the injection of uroselectan showed two small shadows in the right renal area suggestive of calculi.

UROSELECTAN FILMS (*Figs.* 396–399).—

Fig. 396 : Right—a few faint shadows, evidently those of the upper calices, are seen above those of the calculi.
Left—shadow of normal kidney pelvis and calices. The ureter is shown in most of its course and is slightly dilated in its lower third.

Fig. 397 : Right—shadows increased in size and density, showing somewhat dilated calices.
Left—kidney pelvis and calices represented by a fainter shadow than in *Fig.* 396. Ureteric shadow has almost disappeared.
A small, fairly dense shadow is seen in front of the lower part of the sacrum.

Fig. 398 : Right—further increase in density, but not in size, of shadows in renal area.
Left—very faint shadow of kidney pelvis and calices.
The shadow in front of the sacrum has increased in size and density and has spread to the left, evidently due to the dye in the lower part of the pelvic colon.

Fig. 399 : Both renal and ureteric shadows have disappeared.
The large bowel is outlined by a shadow of good density from the rectum to the cæcum, similar in appearance to a barium enema, except for the greater density of the latter.
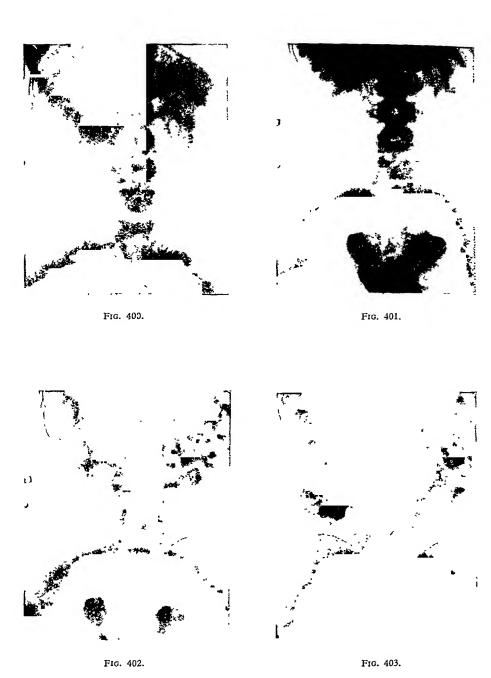
The blood-urea was 46 mgrm. per 100 c.c.

SUMMARY OF CONDITION OF KIDNEYS (14 years and 2 months after transplantation of both ureters). The right kidney contains two or three calculi, and a mild degree of hydronephrosis is present. The shadows shown by the dye indicate that the function of this kidney is somewhat impaired. On the left side, although there is a slight dilatation of the ureter indicating a mild degree of obstruction, the kidney possesses normal structure and function.

FURTHER HISTORY.—Three small calculi were removed from the right kidney in December, 1932. The operation was followed by the development of a persistent sinus and the patient was re-admitted for operation in November, 1933. On this occasion another small stone was removed and after three weeks the wound healed, in which condition it has remained.

LATEST REPORT (April 12, 1935).—The patient writes to say that she is perfectly well. Evacuation of the bowels takes place, on the average, six times during the twenty-four hours, but on one occasion eleven hours elapsed between evacuations.

FIG. 400.

FIG. 401.

FIG. 402.

FIG. 403.

FIGS. 400–403.—*Case* 3.   Uroselectan films taken 5 minutes, $\frac{1}{2}$ hour, $1\frac{1}{2}$ hours, and 6 hours respectively after injection of the dye.

Case 3 (No. 7).—W. P., aged 18 at the time of uroselectan investigation, Nov. 28, 1932.

HISTORY.—The patient suffered from complete epispadias with incontinence. The right ureter was transplanted in August, 1918, the patient then being 5 years of age. After the operation there developed what appeared to be a pelvic peritonitis. Under anæsthesia the lower sutures of the abdominal wound were removed, and as soon as the peritoneal cavity was opened, there was a rush of offensive urine followed by pus. Drainage was provided and the patient steadily improved, being soon well enough to return home. The sinus closed within a few days of his leaving hospital. The left ureter was transplanted in May, 1920. On the tenth day following this operation there was a slight urinary leakage from the site of the abdominal drainage tube ; it continued for a week, when it ceased spontaneously, the remainder of his convalescence being uneventful. The intervening health has been very good.

UROSELECTAN FILMS (*Figs.* 400–403).—

Fig. 400 : Right—kidney shadow large but faint and blurred, indicating an apparent hydronephrosis.
Left—kidney shadow more dense and distinct than on right side and not showing any dilatation.

Fig. 401 : Both kidney shadows show increased density.
Right—the dilated calices are now well defined, showing definite hydronephrosis.
Left—the calices are shown better than on the previous film ; clubbing is seen but there is no dilatation.
There is a faint shadow at the level of the coccyx.

Fig. 402 : Right—the kidney shadow shows increased density ; the ureter is outlined clearly down to the superior border of the sacro-iliac joint and is uniformly and widely dilated.
Left—the density of the kidney shadow is much the same as in the previous film but is somewhat obscured by gas shadows.
The size of the shadow in front of the sacrum is increased and dye is present in parts of the iliac and descending colon.
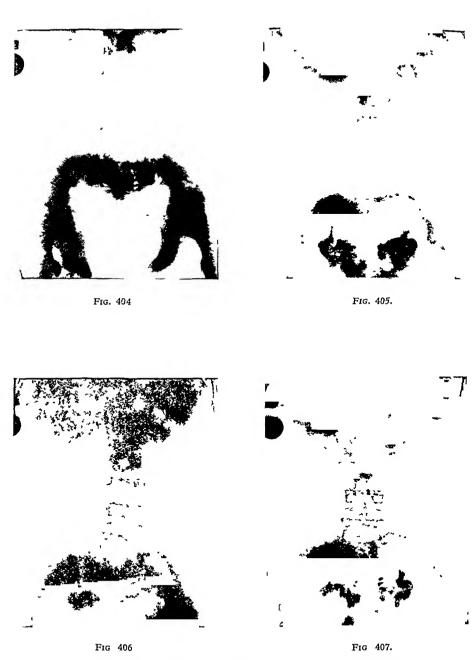
Fig. 403 : Both kidney shadows have disappeared.
Judged by the density of the shadow, the dye is present in good concentration in the cæcum, ascending colon, right third of transverse colon, and the upper portion of the descending colon.

The blood-urea was 48 mgrm. per 100 c.c.

SUMMARY OF CONDITION OF KIDNEYS (14 years and 3 months after transplantation of both ureters).—On the right side there is a well-marked hydronephrosis and hydro-ureter with some impairment of kidney function. On the left side the clubbing of the calices indicates an incipient stage of hydronephrosis. The function of the kidney is good although the degree of obstruction present is sufficient to cause enough dye retention to result in an increased density of shadow up to one and a half hours.

LATEST REPORT (April 10, 1935).—The patient states that he is enjoying very good health. He finds that a bowel movement is generally necessary four times during the day and twice at night, but he has known as long as eight hours elapse between evacuations.

FIG. 404

FIG. 405.

FIG 406

FIG 407.

FIGS 404–407 —*Case* 4   Uroselectan films taken 5 minutes, $\frac{1}{2}$ hour, $1\frac{1}{2}$ hours, and 6 hours respectively after injection of the dye

Case 4 (No. 12).—J. P., aged 19 at time of uroselectan investigation, April 10, 1933.

HISTORY.—Both ureters transplanted in October, 1924, for ectopia vesicæ, the patient being 10 years old. The left ureter was transplanted first and an interval of three weeks allowed to elapse before the right ureter was dealt with in a similar manner. Except for a slight setback soon after the first operation, apparently due to an attack of renal infection which quickly passed off, the patient recovered well from both operations and has enjoyed good health ever since.

UROSELECTAN FILMS (*Figs.* 404–407).—

Fig. 404 : The pelves and calices of both kidneys are clearly shown by shadows of good density ; they are normal, showing neither clubbing nor dilatation.

Right—the upper portion of the ureter is shown and is not dilated ; in the pelvis, just below the sacro-iliac joint a small part of the ureter is seen and is dilated.

Left—that portion of the ureter above the sacro-iliac joint is very faintly outlined and shows slight dilatation ; just below this joint is outlined a small, dilated portion of the ureter turning inwards above the ischial spine.

Low in the pelvis, between the separated pubic bones, a shadow has already made its appearance.

Fig. 405 : Both kidney shadows are less dense.

Right—the outline of the ureter is seen both above and below the sacro-iliac joint ; above, it is slightly dilated, while below, the dilatation is more marked and the ureter is seen to bend inwards.

Left—the ureter is seen only above the crest of the ilium, and, in the middle of this part of its course, shows a slight dilatation.

The shadow in the pelvis has spread upwards and has now reached the level of the lower part of the sacrum.

Fig. 406 : Both kidney shadows are of diminished density and the calices are not so well outlined. Only the upper portions of the ureters may be discerned and with difficulty. The shadow in the pelvis has increased in both size and density.
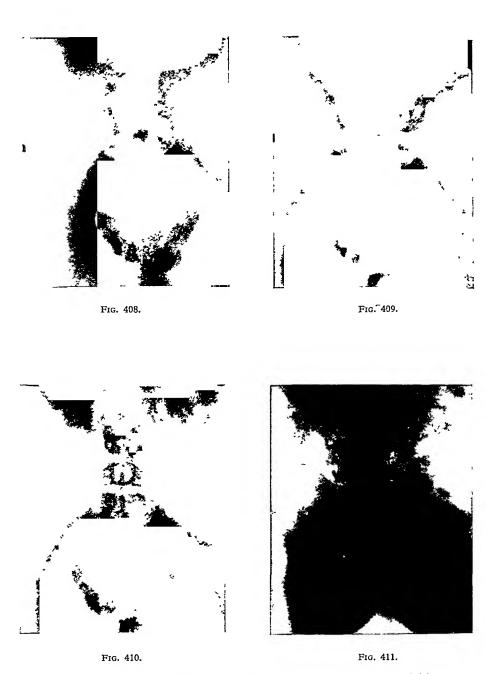
Fig. 407 : Both kidney and ureteric shadows have disappeared. The shadow in the pelvis is not so large or dense as in the last film and no dye is present in the colon.

NOTE.—This boy stated emphatically that he could not allow more than four hours to elapse between evacuations. Because of this, he was instructed to empty his rectum immediately after the third film so as to allow about four hours for further accumulation before the taking of the last film. However, the poor result of the last film shows clearly that almost all the dye had been excreted within one and a half hours of its injection. The details of the ureteric shadows described above, while seen in the original films, are not shown in the photographs.

The blood-urea was 46 mgrm. per 100 c.c.

SUMMARY OF CONDITION OF KIDNEYS (8½ years after transplantation of both ureters).— Both kidneys show a normal structure. While both ureters show some degree of dilatation, the obstruction causing this has not been sufficient to affect the kidneys up to the time of investigation. The manner in which the dye was excreted by the kidneys indicates that each possesses an unimpaired function. It is probable that this case represents as perfect a result as it is possible to obtain.

LATEST REPORT (April 13, 1935).—The patient writes to say his general health is good. He has to empty his rectum about every two hours during the day and generally twice during the night. There is occasional nocturnal incontinence.

FIG. 408.

FIG. 409.

FIG. 410.

FIG. 411.

FIGS. 408–411.—*Case* 5. Uroselectan films taken 5 minutes, ½ hour, 1½ hours, and 6 hours respectively after injection of the dye.

Case 5.—W. C., aged 23 at time of uroselectan investigations, Sept 11, 1931.

HISTORY.—Congenital epispadias with incontinence. Previously several plastic operations performed without success. Left ureter transplanted in February, 1930. Right ureter transplanted in May, 1931. Post-operative notes state that on July 4, 1931, his general condition had much improved and that he had acquired satisfactory control of the rectum. A further note made on Aug. 6 is to the effect that his bowels move on an average four times daily and that he usually passes the night without evacuation being necessary.

UROSELECTAN FILM (*Figs* 408–411) —

Fig. 408 : Right—faint blurred shadow in renal area suggestive of hydronephrosis.
Left—faint kidney shadow showing clubbing and a moderate degree of dilatation of the calices. The ureter is faintly outlined above the ilium, is somewhat tortuous, and definitely dilated.

Fig. 409 : Right—kidney shadow increased in density and showing definite hydronephrosis About an inch of the upper end of the ureter is shown and is dilated.
Left—renal and ureteric shadows less dense.
In the pelvis there is a shadow in front and to the left of the sacrum.

Fig. 410 . In both renal areas the shadows have become less dense and the outlines are indistinct.
Left—the outline of the dilated ureter is again seen faintly in that part of its course above the ilium.
The shadow in the pelvis has increased in size and density, extending upwards in front of the sacrum.

Fig. 411 : Both kidney and ureteric shadows have disappeared The shadow in the pelvis shows a slight increase in size and the large gut is outlined from iliac colon to cæcum by a shadow of varying density.

The blood-urea was 43 mgrm. per 100 c.c.

SUMMARY OF CONDITION OF KIDNEYS (4 months after transplantation of ureters).—Both kidneys show a definite degree of hydronephrosis, more marked on the right than the left, and the ureters are correspondingly dilated While the faint shadows on the first film indicate some impairment of renal function, yet the shadow in the pelvis on the third film shows that quite a good excretion of the dye had taken place at the end of one and a half hours after injection

LATEST REPORT (Aug. 5, 1935) —This patient is now in an institution because of his deteriorated mental condition. His general physical condition is fair. He has to empty the large bowel every two to three hours both day and night Incontinence has occurred but on very rare occasions only

FIG. 412.
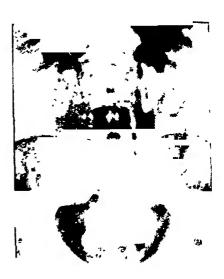
FIG. 413.

FIG. 414.

FIG. 415.

FIGS. 412–415.—*Case* 6. Uroselectan films taken 5 minutes, $\frac{1}{2}$ hour, $1\frac{1}{2}$ hours, and 6 hours respectively after injection of the dye.

Case 6.—Mrs. M. F., aged 35 at time of uroselectan investigation, March 21, 1932. When admitted for this purpose the patient was in excellent health and able to do her daily work.

History.—In 1926 the patient gave birth to a child after a very prolonged and difficult labour necessitating a forceps delivery. She noticed incontinence of urine immediately afterwards. The cause of this was found to be a vesico-vaginal fistula and up to 1930 several operations had been performed for the condition but without success. At this time the opening into the bladder easily admitted a finger. Transplantation of the ureters was advised as the only hope of terminating the miserable condition. The right ureter was transplanted in August, 1930, and the left one a month later. The patient made a good recovery from both operations.

Uroselectan Films (*Figs.* 412–415).—

Fig. 412 : Right—shadow of good density showing normal calices, pelvis of kidney, and the ureter as far down as the transverse process of the last lumbar vertebra.

Left—kidney shadow of good density showing dilatation of both calices and pelvis ; the ureter is outlined as far down as the upper border of the sacrum by a shadow of varying density and is shown to be considerably dilated, especially in its lower part.

Already a faint shadow has appeared in front of the sacrum.

Fig. 413 : Right—kidney and ureteric shadow not quite so dense as in first film.

Left—shadow of both kidney and ureter of increased density ; the lower part of the ureter is dilated in a bulbous manner.

The shadow in front of the sacrum is much denser than in the first film.

Fig. 414 : Right—shadow of kidney and ureter now very faint.

Left—density of kidney shadow increased, that of ureteric shadow diminished. Below the kidney shadow is another, circular in outline—apparently bowel content.

The shadow in front of the sacrum has increased in size and density.

Fig. 415 : Both kidney and ureteric shadows have disappeared. The rectum and lower pelvic colon are outlined by the dense shadow in the pelvis. The dye has reached as high as the splenic flexure of the colon, clearly outlining the iliac and descending portions.

The blood-urea was 44 mgrm. per 100 c.c.

Summary of Condition of Kidneys (18 months after transplantation of ureters).—On the right side, hydronephrosis and hydro-ureter are present in marked degree. In spite of the obstruction which is causing this degree of dilatation, the good density of the shadow in the first film shows that the function of the kidney is good. The left kidney possesses normal structure and function.

In spite of several inquiries made in April and May, 1935, we have been unable to trace this patient again.

FIG. 416.—*Case* 1   Mrs. E. S , aged 41, with her family, all born after transplantation of both ureters into the bowel nineteen years previously.

FIG   417 —*Case* 2   Miss V K , aged 24   In good health 18 years after double transplantation of the ureters

SUMMARY

The results of this investigation of the pathological changes in the kidneys and ureters and the renal function in patients in whom the ureters had been transplanted into the colon are grouped together to form the table below in order that the reader may see them at a glance.

TABLE SHOWING PATHOLOGICAL CHANGES IN KIDNEYS AND URETERS TOGETHER WITH THE RENAL FUNCTION IN 6 CASES OF TRANSPLANTATION OF THE URETERS

CASE No.	RIGHT			LEFT		
	Kidney	Ureter	Renal Function	Kidney	Ureter	Renal Function
1	Hydro-nephrosis	Marked dilatation	Impaired	Normal	Slight dilatation	Good
2	Hydro-nephrosis Calculi	Not shown	Impaired	Normal	Slight dilatation	Good
3	Hydro-nephrosis	Marked dilatation	Impaired	Clubbing of calices	Not shown	Good
4	Normal	Slight dilatation	Good	Normal	Slight dilatation	Good
5	Hydro-nephrosis	Marked dilatation	Impaired	Hydro-nephrosis	Marked dilatation	Impaired
6	Hydro-nephrosis	Marked dilatation	Good	Normal	Normal	Good

Pathological Changes in the Kidneys and Ureters.—The outstanding change in these organs, as demonstrated by the uroselectan pyelography, is dilatation. In only one case (*Case* 6) did a kidney and its ureter appear perfectly normal, but four other kidneys, in *Cases* 1, 2, and 4, also showed a normal structure although the corresponding ureters were slightly dilated. The remaining seven kidneys were the seat of hydronephrosis of varying degree and the corresponding ureters in five of these were much dilated; no ureteric shadow was seen in the other two. It will be noted that in the first three cases the density of the shadow of the right kidney increased progressively in the second and third films, taken ½ hour and 1½ hours respectively after injection, indicating that the uroselectan was being excreted into the lumen of the kidney at a quicker rate than it was escaping into the bowel and thus showing the presence of some obstruction of the ureter. However, in only one of these three cases (*Case* 1) was the obstruction sufficient to have prevented the escape of all the dye from the kidney into the bowel at the end of 6 hours after injection, for a faint shadow of the upper calices and ureter was to be seen in the film taken at this time.

It is known that dilatation of the upper urinary tract may be the result of either obstruction or infection or that both may play a part, but the regularity of the

dilatation shown in the uroselectan pyelograms of these cases points to obstruction as the major causative factor.

In every case the original transplantation had been carried out by imbedding the ureter in the wall of the bowel and without the use of indwelling ureter catheters. Whether the slight obstruction demonstrated by this investigation is caused by the imbedding having been rather too thoroughly carried out or is really cicatricial and the result of a mild infection at the site of the anastomosis it is not at present possible to say. Another explanation, or at least a contributory cause, may be kinking of the ureter where it enters the bowel.

Renal Function.—The uroselectan proved that every kidney was a functioning organ, although in some the function was impaired. In two cases (*Cases* 4 and 6) the shadows of both kidneys on the first films, taken 5 minutes after injection, were of sufficient density to indicate that the dye was being excreted in a normal manner and that therefore the renal function was good. A similar condition was seen in the left kidney in three other cases (*Cases* 1, 2, and 3). In only one case (*Case* 5) did the shadows reveal an impaired function of both kidneys, while impairment of the function of the right kidney only, was noted in *Cases* 1, 2, and 3.

The chief point of interest concerning the impairment of function which had taken place in some of these kidneys lies in the fact that in none could it be considered gross, for in none was there a complete failure to excrete the dye. Further proof of this is apparent in the third films taken at the end of $1\frac{1}{2}$ hours after injection; in all of these a shadow of good density is present in front of the sacrum, indicating that much of the dye has already been excreted by the kidneys and has passed into the rectum and lower part of the pelvic colon.

Blood-urea.—The values of the blood-urea in these cases lie between 35 and 48 mgrm. per 100 c.c. They are of interest because in the presence of such definite obstructive changes one might reasonably have expected higher values. They are, moreover, in agreement with the renal functions as indicated by the uroselectan and also with the general good health of these patients.

Renal Infection.—While, as previously mentioned, it is probable that in every case of transplantation of the ureters an ascending infection of the kidney takes place in some degree, yet evidence obtained in this investigation indicates that in the cases under review it must exist in only a very mild form, for the dilatation shown by the pyelograms is obstructive in type and does not bear the irregular characteristics of that due to infection. Furthermore, it is unlikely that severe renal infection would be accompanied by such a small degree of impairment of renal function and such low blood-urea values.

The Rôle of the Large Bowel in the Storage of Urine.—It is interesting to trace, through the shadows produced on the films by the uroselectan, the part played by the large bowel in the storage of the urine. In every case, an appreciable amount of urine had collected in the rectum at the end of half an hour after the injection of the dye. In another hour the urine had filled the rectum, and its level had begun to ascend into the pelvic colon, occupying its lower portion. By the end

of the sixth hour the urine, in four cases, had found its way back as far as the cæcum, and in another had risen to the level of the splenic flexure.

These films present, in a pictorial manner, convincing proof that, in cases where the ureters have been transplanted into the colon, not only the rectum but the remaining portion of the large bowel can, and does, act as the reservoir for the urine, and they explain at once why these patients can allow such lengthy intervals to elapse between evacuations.

We are much indebted to Dr. Whately Davidson, Honorary Radiologist to the Royal Victoria Infirmary, Newcastle-upon-Tyne, for the interest he took in these cases and for the help he gave us on many occasions.

REFERENCE

[1] TURNER, G. GREY, " The Treatment of Congenital Defects of the Bladder and Urethra by Implantation of the Ureters into the Bowel : with a Record of 17 Personal Cases ", *Brit. Jour. Surg.*, 1929, xvii, 114.

A GRIDIRON ACCESS TO THE BILIARY APPARATUS

BY C. JENNINGS MARSHALL

SURGEON, CHARING CROSS HOSPITAL

THE very multiplicity of incisions for approach to the gall-bladder and bile-ducts suggests the relatively unsatisfactory character of all, or at least an absence of general applicability to biliary cases. The paramedian is adequate in thin subjects and has the advantage of extensibility without parietal mutilation (surely discounted nowadays when the abdomen is opened on much more precise indications than formerly); the outer rectus incisions need extensions and are liable to nerve damage—their suture in the usual gall-stone case is difficult, particularly so in the instance of the posterior sheath, where the stitches cut out of the fatty atrophied tissue along the line of the fibres on the slightest tension; the paracostal incision of Kocher is nerve-murderous and bloody; the transverse incision of Maylard is sound with regard to the relationship between tension and the line of incision (wherein the vertical incisions are great offenders), but the division of the rectus is troublesome and bloody.

The approach here suggested is claimed to be :—

1. Preservative of parietal innervation.

2. Particularly easy of suture even with a straining patient, the stitches having no tendency to cut out.

3. Adequate in all cases, the access being equal to that in the Kocher method.

4. A gridiron access permitting the patient to get up very early without the slightest danger of bursting the wound.

5. Suitable for dealing with the appendix either through this incision or by a simple modification.

TECHNIQUE

1. The incision should reach the anterior sheath of the rectus $\frac{1}{2}$ to $\frac{3}{4}$ in. to the inner side of the outer edge of this muscle; where this is palpable the cut can be made accordingly, otherwise it passes downwards vertically from the region of the eighth costal cartilage for a distance appropriate to the habitus of the patient, varying from 5 to 8 in.

2. The anterior sheath is incised $\frac{1}{2}$ to $\frac{3}{4}$ in. inside the outer edge of the rectus; the margins of the outer flap being held by forceps; this is reflected outwards from the muscle, the inscription offering difficulty and several bleeding points having to be secured.

3. The crux of the access now is reached; the *posterior lamina of the internal oblique contribution to the rectus sheath is incised as it passes to the transversalis* (a muscle showing considerable variety in its formation of the upper part of the sheath), throughout the whole length of the incision (*Figs.* 418, 419). The oblique muscles are now found capable of wide retraction from the surface of the transversalis.
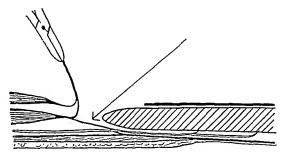
FIG. 418.—Shows the posterior lamina of the internal oblique aponeurosis perforated by an intercostal nerve. The line of section is indicated by an arrow.

FIG. 419.

FIG. 420.
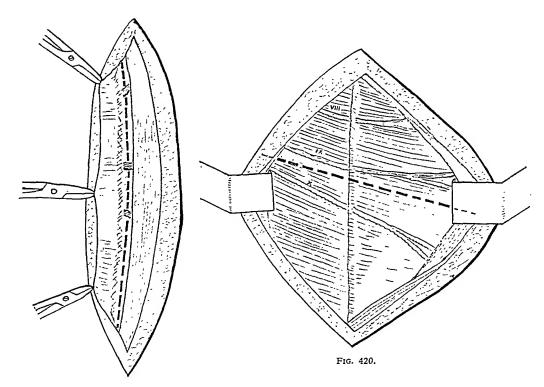
FIG. 419.—The outer flap of the rectus sheath drawn outwards, showing the splitting of the internal oblique aponeurosis (criss-cross line) and the position of incision in posterior lamina broken line).

FIG. 420.—Rectus and obliques retracted; the transversalis with the eighth, ninth, and tenth nerves and accompanying arteries and veins are seen. Incision of transversalis indicated by broken line.

4. The obliques and the rectus, freed by gauze, are widely retracted (the rectus, if very wide, may need some division from the seventh cartilage). The eighth, ninth, and tenth nerves are seen ; the transversalis is divided almost transversely between the latter pair, which emerge close together from the costal margin ; the division extends from the mid-line to the region of the tenth costal cartilage (*Fig.* 420).

FURTHER OBSERVATIONS

1. If the cæcum and appendix are not mobile, the latter may be dealt with by extending the division of the anterior sheath and posterior lamina to a lower level, and making an appropriate transverse incision in the posterior sheath.

2. Paramedian incision and *transverse division* of the posterior sheath gives adequate access and perfect safety from wound-bursting in cases of perforated duodenal ulcer.

3. The *posture of the patient* for biliary operations is ideally a sort of inverted Trendelenburg, but this is difficult of maintenance in the diffluent sort of patient usually met with in these cases ; the essential is that gravity should be utilized to remove the intestine from the field of operation ; hence the thorax and head of the patient may be on a level (supported by sand-bags and the bridge), the abdomen inclined downwards at an angle of 40° to 50°, and the lower limbs level. The bridge on the operating-table, if ever so slightly malposed, will cause the ducts to be drawn up into the thorax, and greatly intensify the difficulty of the operation.

MUCOID CARCINOMA OF THE CÆCUM IN A BOY OF 13 YEARS

By ROBERTSON F. OGILVIE

FROM THE PATHOLOGICAL DEPARTMENTS OF THE UNIVERSITY AND ROYAL INFIRMARY, EDINBURGH

A REVIEW of the literature reveals a comparative dearth of reported cases of carcinoma of the colon in childhood. The following have been found :—

AUTHORS AND DATE	SITE IN COLON	AGE IN YEARS	SEX
Ball, H. A. (1935)	Sigmoid flexure*	15	F
Chajutin, D. M. (1929)	Cæcum	14	F
Clar	—	3	M
Desaive, P. (1934)	Anorectal	13	—
Garrard, W. A. (1897)	Sigmoid flexure*	12	M
Kanthack, A. A., and Furnivall, P. (1896)	Ascending colon*	17	M
Lawson, T. C. (1934)	Rectum	17	M
Nothnagel, H. (1898)	Cæcum	12	M
Pouzet, F. (1933)	Ascending colon	14	M
Raiford, T. S., and Buttles, E. M. (1933)	Rectum*	13	F
Rocher, H. L., and Guerin, R. (1931)	Splenic flexure	11	—
Schöning (2 cases)	Rectum (both)	17 (both)	F (both)
Wakeley, C. P. G. (1933)	Ascending colon	16	M
Walker, R., and Daly, J. F. (1934)	Cæcum	5	M

* Showed mucoid degeneration.

It is apparent that carcinoma of the cæcum in childhood is a rarity, and hence the present case seems worthy of record. After this case was described to the Edinburgh Pathological Club my attention was directed to a further instance of carcinoma of the (transverse) colon in a 15-year-old boy who was admitted under the care of Mr. Stuart in the Royal Infirmary, Edinburgh, in 1935.

HISTORY.—The patient was a schoolboy aged 13 years. Five days before admission he complained of severe pain in the right iliac fossa, the onset of which was shortly followed by vomiting. On the following day he was comparatively well, but three days before admission the pain and vomiting recurred and continued intermittently until he was admitted under the care of Mr. Struthers in the Royal Infirmary, Edinburgh. On the day of admission (Dec. 31, 1934) the patient's bowels moved twice. There was no history of any bladder trouble.

ON ADMISSION.—The boy's temperature was 99·2° F., his pulse was 80 per minute, and his respirations 22 per minute. His general condition was poor and he was obviously anæmic. His tongue was furred, but moist. His abdomen moved freely on respiration and showed neither distension nor peristalsis, but a swelling was visible in the right iliac fossa. On palpation this was found to be firm and tender and guarded by resistant muscles.

OPERATION.—On Jan. 1, 1935, the abdomen was opened through a gridiron incision in the right iliac fossa. A smooth, firm swelling was found in association with the cæcum, and some enlarged glands were found in the mesentery. On the basis of these findings a diagnosis of hypertrophic tuberculosis of the cæcum was made and an anastomosis was carried out between the lower part of the ileum and the middle of the transverse colon.

SUBSEQUENT HISTORY.—Convalescence was uneventful. The swelling in the right iliac fossa did not diminish, but became less tender and the patient's general condition improved greatly. He was sent to convalesce at the Astley Ainslie Institution on Feb. 12.

From the institute the patient was returned to the infirmary on April 10 with a history of having on that date had a recurrence of abdominal pain and vomiting. Following admission he was sick several times, but an enema produced a good result, and except for slight abdominal pain there were no further complaints. During the night and day following admission he had about fifteen fits, which appeared to begin on the left side and spread over the body. The contractions, at first clonic in character, became tonic, and were accompanied by partial loss of consciousness. After the last fit at 9.10 p.m. on April 11 he became drowsy, and though Kernig's sign remained negative definite neck rigidity was detected.

Thereafter the patient had no more fits, and after three days the drowsiness and neck rigidity disappeared. A small lump developed in the left occipital region, but apart from occasional headaches he remained well and was discharged again to the Astley Ainslie Institution on April 30. Whilst there his condition deteriorated ; he lost weight, complained of spinal pain, became drowsy, and on May 10 he took three fits characterized by twitching of the right side of the face and of the eyes to the right side and by partial loss of consciousness. On lumbar puncture the cerebrospinal fluid was found to be under pressure and slightly turbid, but no tubercle bacilli were found.

He was re-admitted to the infirmary on May 14. The lump at the back of the head had enlarged and fluctuation could be elicited in it, but it was not tender. The scalp was movable over it, yet the lump itself appeared firmly fixed to the underlying bone. From the swelling a chain of enlarged glands extended down into the neck. He complained of pain in the neck, and though no actual neck rigidity was present he resisted attempts to lift his head. There was tenderness over the last cervical and first thoracic vertebræ. Kernig's sign was positive on both sides, but the pupillary, knee, ankle, and plantar responses were normal. Physical examination revealed nothing abnormal in the chest. X-rays revealed an area of lessened density in the occipital bone, nothing abnormal in the vertebral column, and diffuse mottling throughout the right lung, most marked at the hilum.

A needle was inserted into the occipital lump, but nothing could be aspirated. The swelling steadily increased. Twice he passed stools containing bright red blood, and continually complained of severe abdominal pain which necessitated heroin. On May 17 he had rigors and his temperature rose to 103°. Thereafter his temperature fell, but remained irregular. On May 21 he had a fit. His general condition deteriorated rapidly, he sweated profusely, became emaciated, and died on May 22. Clinically death was attributed to tuberculous meningitis.

POST-MORTEM EXAMINATION.—

. *Macroscopical.*—The body was that of a rather emaciated boy. The abdomen was somewhat prominent, and a long, oblique, well-healed scar was present in the right iliac fossa. On opening the body the peritoneal cavity was found to be congested, especially in the lower quadrants, where there was some purulent exudate. Over the liver and diaphragm a number of small yellow nodules was seen in the serous membrane. The ileocolic anastomosis was apparently healthy.

The pleural sacs were partly obliterated by fibrous adhesions, and a small quantity of serous fluid was present in each.

The cæcum was hard to the feel, but not enlarged. On section its wall was found to be replaced by a dense yellowish-white mass which completely surrounded the narrow lumen (*Fig.* 421). The infiltration also involved the ileocæcal valve and
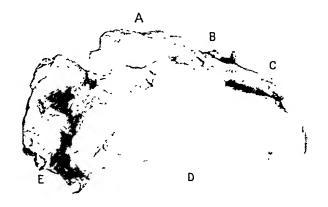
FIG. 421.—A, Cæcum with walls much thickened by malignant growth which has spread proximally through the ileocæcal valve (B) to involve the terminal ileum (C); D, A mass of lymph-glands replaced by neoplasm; E, Ascending colon showing precipitous margin of cæcal growth at proximal end.

the terminal $1\frac{1}{2}$ in. of the ileum, where it gradually faded away. The distal margin of the cæcal mass, on the other hand, was precipitous and well defined. The inner surface of the cæcum was ulcerated and hæmorrhagic. In the ascending colon just distal to the neoplasm two or three small nodules suggesting secondary implants were found in the mucosa. The appendix, though swollen, did not appear to be involved.

The glands in the ileocæcal angle were enlarged and on section were found largely replaced by tumour tissue in which areas of necrosis were present. Lymph-node involvement was also found in the para-aortic, omental, and bronchial glands.

The spleen was enlarged and soft. The stomach, liver, gall-bladder, pancreas, kidneys, ureters, and bladder showed nothing of note. The heart was dilated and the myocardium pale and soft. Throughout the lungs were scattered a few small firm nodules of tumour tissue.

On removing the skull there was no evidence of meningitis, but small nodules of tumour were present in both anterior and posterior fossæ and in the right middle fossa. The largest skull-deposit measured $4\frac{1}{2}$ cm. in diameter and was found in the left occipital region. It had grown so as to produce fairly large masses of gelatinous

tissue both external to the dura (*Fig.* 422) and under the scalp. The mass in the latter situation represented the swelling which had been aspirated during life. Apart from considerable œdema, the brain showed nothing of note.
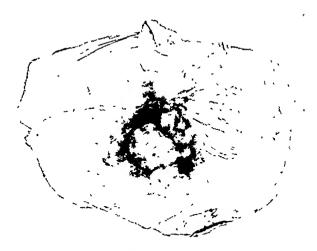
FIG. 422.—Dura from left occipital region with mass of gelatinous growth attached to its external surface. In the immediate neighbourhood of the mass are several small subsidiary nodules.

Microscopical.—The wall of the cæcum from mucosa to peritoneum was infiltrated by a spheroidal-celled carcinoma. Many of the cells showed the ' signet-ring ' appearance of mucoid degeneration, and occasionally small masses of mucus

FIG. 423.—Cæcum showing infiltration of its muscular coat by spheroidal-celled carcinoma. Some of the cells have the ' signet-ring ' appearance of mucoid degeneration, and to the right is a mass of mucus almost devoid of cells. (× 120.)
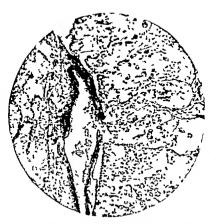
FIG. 424.—Lung showing perivascular lymphatic spread of the carcinoma. To the right of the vessel is a mass of spheroidal-celled growth in a state of advanced mucoid degeneration : to the left is œdematous lung tissue. (× 50.)

devoid of cells were present between the muscle-bundles (*Fig.* 423). The surface of the growth was necrotic, ulcerated, and much congested.

A bronchial gland showed almost complete replacement of its substance by spheroidal-celled neoplasm undergoing early mucoid change.

Sections of lung demonstrated a perivascular lymphatic spread of the growth (*Fig.* 424). The latter was spheroidal-celled and in a state of advanced mucoid degeneration. From the lymphatics the neoplastic tissue had spread by direct infiltration into the adjacent lung tissue so that nodules of considerable size had been formed. The wall of a fairly large vein was seen being invaded by tumour-cells (*Fig.* 425).

FIG. 425.—Lung showing perivascular lymphatic spread of the carcinoma. The spheroidal-celled mass to the right has invaded the wall of the adjacent vein. (× 50.)

FIG. 426.—Scalp nodule in left occipital region showing a large thin-walled vessel surrounded by mucoid growth and containing a malignant embolus in its lumen. (× 120.)

The scalp nodule consisted of spheroidal-celled tissue in a state of advanced mucoid degeneration. Two or three thin-walled blood-vessels showed small masses of tumour-cells within them (*Fig.* 426).

Liver showed fatty change but no secondary deposits.

COMMENTARY

The outstanding feature of the case is the age of the subject. During the ten years 1920–9 inclusive 322 cases of carcinoma of the colon, excluding rectum, were admitted to King's College Hospital and the average age of the patients was 52 (Wakeley, 1933). In 100 cases of carcinoma of the cæcum collected from the Mayo Clinic by Craig and MacCarty (1923) the average age incidence was 49, while in 25 cases of cæcal carcinoma operated on by Wakeley (Wakeley and Rutherford, 1932) the average age incidence was 58. No doubt the rarity of the condition at the age of 13 years was largely responsible for the way in which the surgeon was misled in making a diagnosis of hypertrophic tuberculosis of the cæcum, and it is interesting that the provisional clinical diagnosis in Ball's (1935) case of carcinoma of the sigmoid flexure in a girl of 15 was tuberculous peritonitis.

The mode of spread throughout the greater part of the illness appears to have been lymphatic—first to the regional mesenteric glands and thence by the para-aortic to the glands of the lesser omentum and to the bronchial glands, whence there was perivascular spread into the lungs. A pulmonary vein in process of being eroded was observed microscopically and it is likely that it was by such a process that invasion of the blood-stream occurred and metastases in the skull ensued. The

absence of secondary growths in the liver is noteworthy, but by no means exceptional in cases of cancer of the colon. This case is thus similar to that of Raiford and Buttles (1933), which was also characterized by skull metastases but no liver involvement.

Mucoid degeneration was an outstanding feature of the growths in this case, particularly of that in the occipital region. Such a change is a fairly common characteristic of colon carcinomata arising in the later years of life, and it would appear to be equally common in the earlier years. Thus of the 17 cases mentioned in this paper 5 exhibited the phenomenon.

I am indebted to Mr. Struthers for permission to publish this case.

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ANTERIOR DISLOCATION OF THE HIP

By J. A. MacFARLANE, Toronto

On the evening of Feb. 25, 1934, a schoolboy, aged 17, was admitted to the Toronto General Hospital complaining of severe pain in the left groin and inability to walk. About three hours previously he had fallen while ski-ing. He was going down a partially wooded hill and his left ski caught in some underbrush while he was

FIG 427.—Anterior dislocation of the hip.

travelling at a good speed. He found himself lying prone, with his head down the hill, his right ski free of his foot and his left one turned out. The accident happened so quickly that he could not describe it more fully. He found he was unable to walk and had pain in the region of the hip-joint.

The boy was seen in the X-ray Department of the hospital, lying on a stretcher. The left leg was externally rotated and it appeared slightly longer than the right.

Measurements revealed no appreciable difference in the length of the limbs. The left thigh was in complete extension. There was no apparent adduction or abduction. There was a rounded prominence evident below Poupart's ligament. Active and passive movements at the hip-joint were absent. A diagnosis of anterior dislocation was made and X-ray plates confirmed this diagnosis. (*Figs.* 427, 428.)

The patient was placed on a mattress on the floor, given ether anæsthesia forthwith, and an attempt was made to reduce the dislocation. All attempts at reduction failed, and after thirty minutes of effort the patient was sent to the ward.

FIG. 428.—X-ray appearance of anterior dislocation of the hip.

On the following morning the physical findings were unchanged except for the presence of considerable bruising on the left groin. The boy was then anæsthetized again with full ether anæsthesia, and in the presence of several of the surgical staff further attempts at reduction were undertaken. The manipulations carried out were those described by Bigelow for anterior dislocations. The thigh was first flexed and pulled down, counter-extension being applied by a folded sheet around the opposite thigh and held by an assistant. With the thigh flexed and pulled down, pressure was applied over the prominence of the head, attempting to push it downwards and backwards as the thigh was rotated. These manipulations were carried out repeatedly by several surgeons in turn. At the end of forty-five minutes it was decided that further attempts were useless and might cause additional harm.

Two days later an open operation was carried out through a Smith-Petersen incision. The structures arising from the anterior part of the iliac crest were removed subperiosteally and retracted laterally, the sartorious retracted medially. This procedure exposed the head of the femur partially covered by some torn fibres of the rectus femoris. When this structure had been retracted laterally one tried to discover whether any muscular structure had slipped behind the head preventing its reduction. The psoas tendon was in its proper position and the dislocation seemed to be through the capsule between the medial border of the Y ligament and the pubocapsular ligament. Manipulations at this stage failed absolutely to dislodge the head from its position on the pubic ramus. The neck of the femur was further exposed by cutting the capsule towards its femoral attachment, and, in so doing, part, at any rate, of the medial limb of the Y ligament was cut. It was then possible to pass a long skid down into the acetabulum in front of the head and by combined efforts of flexion and pressure downwards on the head, guided as it was on the skid, and levered away from the pubic ramus, reduction was finally effected. The rent in the capsule appeared as indicated in *Fig.* 429.

FIG. 429.—Appearance of hip after reduction.

The boy's convalescence was uneventful and he was discharged from the hospital in four weeks, walking with crutches. At the end of seven weeks he was allowed to walk without support. On Nov. 28 he was examined again. There was no limitation of motion in any direction and he was satisfied he could do anything he did previous to the accident. X-ray examination at this time showed no evidence of change in the femoral head. Examination in January, 1935, confirmed the findings of November, 1934 (*Fig.* 430). X-ray examination, however, at this time showed a little flattening of the head in the area of attachment of the ligamentum teres (*Fig.* 431).

COMMENT

Traumatic dislocation is a relatively rare injury. The dislocated head may go forwards or backwards. Posteriorly the head may be above or below the tendon of the obturator internus. Anteriorly it may be in the obturator foramen, it may rest on the pubic ramus, or it may be just below the anterior superior spine. I have personally treated only three cases of traumatic dislocation, two posterior ones and the case reported—a suprapubic one. In the files of the Toronto General Hospital there are only 26 cases of traumatic dislocation and these were all anterior.

Dr. R. M. Wansbrough has kindly allowed me to look into the records of the Children's Hospital for the past ten years. During that time there were four cases of posterior and one of anterior dislocation. Choyce[1] reported 59 cases of traumatic dislocation in children, this being the entire number in the literature reported up to that time. Three were suprapubic, one of which was reduced

Fig. 430.—X-ray appearance after reduction (November, 1934).

Fig. 431.—X-ray appearance after reduction (January, 1935).

immediately, and two of which necessitated open operation two and a half and three months following the injury. E. J. Smith[2] reported a case of suprapubic dislocation treated successfully by manipulation seven hours after the injury.

There are several reports in the literature of the treatment of late cases of traumatic dislocation, but I have not been able to find a case record which notes the difficulties which may be encountered in immediate reduction of suprapubic dislocations. Bigelow, in his monograph on dislocation of the hip states, " I have never met with suprapubic dislocation in the living subject and am therefore unable to speak of the extent of a difficulty of flexion alluded to by some writers as characteristic of this luxation." His experimental work on the cadaver led him to believe that this dislocation like all others might successfully be treated by manipulation.

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CALCIFIED   CYST   OF   THE   PERICARDIUM

By A. DICKSON WRIGHT, London

CALCIFIED cysts of the pericardium are of sufficient rarity to warrant presentation of the following case.

A young man, a rubber planter, aged 25, had received a heavy blow on the chest while playing Rugby football in the tropics. Persistent pain after the injury resulted in an X-ray being taken, and the extraordinary calcified shadow shown in *Fig.* 432 was discovered. The patient was shown the X-ray and from then on
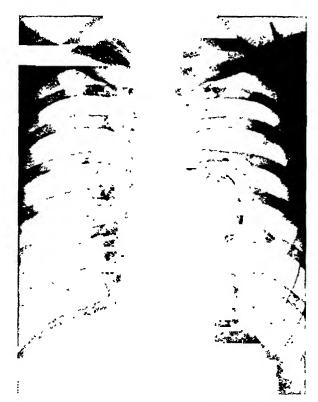
FIG. 432.—Antero-posterior view to show the position of the tumour. The lateral view showed it to be lying in contact with the anterior chest wall.

developed fluttering and disagreeable sensation in the region of the heart; he was referred to me with a view to having the tumour removed. There was one significant fact in his history in that seven years previously while playing hockey he had received such a severe blow with the ball over the heart that he became unconscious for some hours and was in bed for a week, taking two months to get quite well.

On the X-ray screen the tumour gave a most remarkable appearance of moving with the heart-beats. Artificial pneumothorax was induced to see if the tumour

moved with the collapsed lung, but as it did not do so it was inferred that it was attached to the pericardium. It was interesting to note that the pneumothorax greatly increased the fluttering sensations in the chest, probably because of the increased mobility of the tumour no longer surrounded by lung, and this was borne out on screening the patient, when the movements of the tumour were much accentuated.

OPERATION.—A transverse incision was made in the 5th intercostal space anteriorly, and the 5th and 6th costal cartilages and the 6th rib in the anterior axillary line were divided to increase the spread obtained with a Nelson rib retractor. The internal mammary artery was doubly ligated and the pleural cavity opened widely, and the tumour presented a most remarkable sight as it danced wildly about with the ventricular pulsation. The tumour was steadied with Allis forceps and
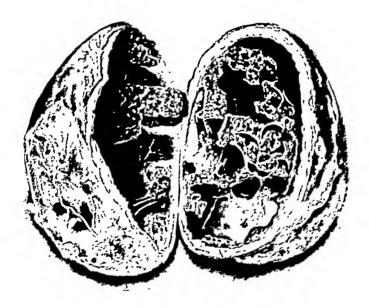
FIG. 433.—The cyst sawn through. The facet which contacted with the chest wall can be seen on the left half of the cyst.

an incision made round its base, the tumour being shelled out from its capsule. Two arteries required ligature in the bed of the tumour and it was then noticed that the pericardial cavity had not been opened, so that the tumour lay between the layers of the pericardium. The mediastinal pleura was sewn up with a continuous fine catgut stitch and the pleura was closed with pericostal sutures. A stab-drain was left through a rib space posteriorly, a mushroom-headed catheter being used for this purpose. This drain was water-sealed and yielded 10 oz. of blood-stained fluid in the first twenty-four hours ; the drainage then ceasing, the tube was removed after forty-eight hours.

Recovery was uneventful, and the patient has remained fit and well ever since and again plays Rugby football regularly within a few miles of the equator.

PATHOLOGY.—The tumour (*Fig.* 433) was strong and hard and had a facet on

one surface where it was presumed it rubbed against the chest wall. To open it a hack saw was used; it had a wall $\frac{1}{4}$ in. thick and contained a loculated brown mass of amorphous material with a beige-coloured fluid in the interstices, which fluid glistened with cholesterin crystals. The chemical examination of the fluid made by Dr. Roche Lynch showed the presence of an appreciable amount of iron; under the microscope crystals of cholesterin and calcium phosphate were numerous; no hooklets, hairs, or keratin were found.

Dr. W. B. Newcombe examined the structure of the cyst wall (*Figs.* 434, 435) and found it to consist of laminated fibrous tissue impregnated with calcium salts, and it was his opinion that the tumour was a calcified blood cyst.
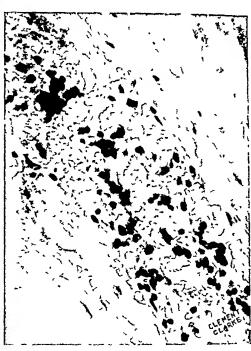
FIG 434 —Low-power view of the wall of the cyst, showing the laminated arrangement of the fibrous tissue   There was no endothelial or epithelial lining to the cyst

FIG 435 —High-power view of the cyst wall, showing the breaking up of the collagen fibrils and calcareous particles not removed in the process of decalcification

Comment.—This case is an unusual manifestation of the well-known tendency for calcification to occur in the pericardium. The sequence of events was that the blow with a hockey ball in 1926 caused a large extravasation of blood between the layers of the parietal pericardium. The amount of blood was more than the local histiocytes could absorb, with the result that a large more or less spherical collection of semi-clotted blood was left between the layers of the pericardium. The irritation produced by this caused an adventitious fibrous capsule to be formed, which, like other chronic pericardial lesions, became calcified, and the blood contained in the chalky capsule could not be absorbed and in the slow process of years changed into cholesterin and other substances, but retained still a brownish colour from the blood pigments.

A CHLORIDE-SECRETING PAPILLOMA IN THE GALL-BLADDER

A TUMOUR OF HETEROTOPIC INTESTINAL EPITHELIUM CONTAINING PANETH CELLS AND ENTEROCHROMAFFINE CELLS AND ASSOCIATED WITH MASSIVE CHLORIDE LOSS : WITH A CRITICAL REVIEW OF PAPILLOMA OF THE GALL-BLADDER

By ARCHIBALD B KERR

EXTRA DISPENSARY SURGEON, THE WESTERN INFIRMARY, GLASGOW

AND ALAN C LENDRUM

ASSISTANT PATHOLOGIST, THE UNIVERSITY AND WESTERN INFIRMARY, GLASGOW

THE case to be described is one of cholecystostomy for presumed mucocele in which, during a drainage period of thirty-four days, there was an excessive outpouring of chloride and water ; the source of this fluid was revealed only on subsequent cholecystectomy, when there was found in the gall-bladder a papilloma composed of intestinal epithelium. It is presented in detail on account of the difficulties in diagnosis, the peculiar biochemical behaviour, and the unique underlying pathology.

CASE REPORT

HISTORY —A labourer, aged 64, was admitted to the Western Infirmary, Glasgow, on Oct. 30, 1934, under the care of Mr. Roy Young. He complained of constipation and of a swelling in the abdomen During the preceding ten weeks he had noticed increasing constipation though his bowels had previously been regular. He first became aware of a swelling in the upper right abdomen three weeks prior to admission, and this did not, to his knowledge, vary in size during the intervening period. His appetite had recently been poor and he had been much troubled by flatulence and sour mouthfuls. He was losing strength and weight No symptoms referable to the urinary system were elicited. He had suffered from pneumonia twenty and ten years previously. The family history was good

ON EXAMINATION.—The temperature and pulse-rate of the patient were normal. He did not look acutely ill but was frail and his appearance suggested that he had lost some weight. There was no jaundice.

The right side of the abdomen was rather prominent and a smooth firm mass was palpable extending from the costal margin above to just below the intercristal line, and from the right flank to the middle line. The mass was not tender, was dull to percussion, and moved fairly freely with respiration and on manipulation. It could not, however, be readily pushed forward from the posterior lumbar region. The liver dullness was found to be normal except where its continuity with the dullness of the mass prevented the definition of its lower margin. There was slight epigastric tenderness.

Varicose veins were noted in the left leg. Occasional crepitations were heard at the base of the left lung. The heart and nervous system presented no abnormalities. The urine was normal and the Wassermann reaction was negative.

A barium enema passed freely to the cæcum. The mass was reported to lie medial to the cæcum and ascending colon and below and behind the transverse colon. It was not attached to any portion of the colon.

Cystoscopy and right-sided pyelography failed to reveal any abnormality in the urinary tract.

DIAGNOSIS.—In view of the paucity of symptoms, the diagnosis rested largely on the objective findings. Despite the marked constipation the barium enema appeared to eliminate primary disease of the colon. The mass seemed to lie too far forward to have its origin in the right kidney and this was supported by the pyelographic findings. The upper end of the mass was thought to pass too deeply for a cyst or tumour of the liver, and, though muco-cele of the gall-bladder was considered with some favour on clinical grounds, the observation that the mass lay behind the barium-filled transverse colon appeared to exclude this condition. The pre-operative diagnosis was thus of a cystic or solid tumour of the mesentery or possibly of a pancreatic cyst. The radiological observation, however, that the mass lay behind the colon was proved at operation to be fallacious.

FIRST OPERATION.—On Nov. 20, Mr. Roy Young operated under general anæsthesia. Through an upper right rectus incision, he found the mass to consist of an enormously
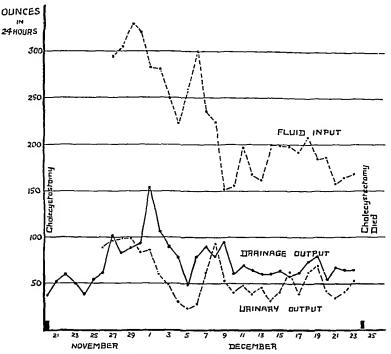
FIG. 436.—Chart showing drainage output from the gall-bladder, urinary ou put, and fluid input (including intravenous input) during the period of drainage.

distended gall-bladder occupying the usual site in front of the colon. Over 20 oz. of clear colourless fluid were aspirated. The gall-bladder was then incised and 10 oz. of thicker dirty fluid were removed along with eight rather flattened opalescent gall-stones. The patient's general condition was giving rise to some anxiety and drainage of the gall-bladder was there-fore adopted in preference to its removal.

The fluid from the gall-bladder showed no organisms in films or on culture.

The centre of each calculus was found to consist of bile pigment admixed with a small proportion of calcium salts, while the pearly outer coating was of almost pure cholesterol. No unusual constituent was found.

POST-OPERATIVE COURSE.—During the twenty-four hours succeeding operation, 38 oz. of fluid, thin and at first somewhat blood-stained, drained from the gall-bladder. Thereafter the discharge continued as a clear and quite colourless watery fluid, and during the third day its amount reached 60 oz. in twenty-four hours (*Fig.* 436).

During this period the patient's general condition was satisfactory apart from cough and muco-purulent expectoration, but it gradually deteriorated, and by the fifth day (Nov. 25) he was obviously distressed. Cyanosis, pallor, and irregularity and weakness of the pulse indicated the onset of cardiac failure, while his pinched face, sunken eyes, and dry tongue pointed clearly to dehydration despite the fact that he had been drinking freely. The similarity of the clinical picture to that of intestinal obstruction led to an examination of the urine for chlorides. The urine contained practically no chlorides. In marked contrast to this was the finding in the drainage fluid of abundant chlorides. The intravenous administration of 2 pints of 2 per cent sodium chloride was followed within an hour by dramatic clinical improvement and the early re-appearance of chlorides in the urine. From this point saline was given by mouth in addition to water, and the total fluid input and urinary output were recorded (*Fig.* 436).

Quantitative estimations two days later (Nov. 27), gave the following results :—

	URINE	DRAINAGE FLUID
NaCl ..	.. Trace	.. 0·79 per cent
Urea ..	.. 1·6 per cent ..	.. Not examined
NaHCO₃	.. Not examined	.. Negligible

Although chlorides were already practically absent from the urine, it was not until the following day that the patient's clinical condition again began to deteriorate, and by Nov. 30 he again showed all the adverse signs noted on Nov. 25. A similar intravenous injection of saline was therefore given and the clinical improvement was as striking as on the first occasion.

Until Dec. 24, a total period of thirty-four days, his condition was satisfactorily maintained and even improved by a series of such saline injections, each necessitated by the recurrence of the same group of symptoms at intervals of five or six days. The drainage amounts for this period, including the extraordinary peak figure of 7¾ pints on the eleventh day, are seen in *Fig.* 436.

The blood-urea was found on Dec. 7 to be 0·039 per cent.

Biochemical examinations immediately before intravenous injection on Dec. 11 gave the following results :—

	URINE	DRAINAGE FLUID			BLOOD PLASMA.
NaCl ..	.. Trace ..	.. 0·81 per cent	..	..	0·52 per cent
Urea ..	.. 1·7 per cent ..	Not examined	..	..	Not examined

The drainage fluid was examined bacteriologically on Dec. 1. Abundant pus cells were found and a coliform organism was isolated and later identified as a paracolon bacillus.

SECOND OPERATION.—On Dec. 24, Mr. Roy Young again operated, on this occasion under spinal anæsthesia. The gall-bladder was freed from omental adhesions and removed without much difficulty. The patient's condition appeared satisfactory after the operation, but a few hours later he became very restless and noisy. His pulse weakened and he died eighteen hours after cholecystectomy. Permission for a post-mortem examination could not be obtained.

PATHOLOGICAL REPORT ON GALL-BLADDER

The gall-bladder (*Fig.* 437) forms an elongated sac, 16·5 cm. long by 10 cm. in maximum circumference, the fundus or distal end being somewhat narrower and showing the drainage opening. The external surface is in general smooth, but omental adhesions are noted at the fundus and also near the middle of the specimen, where there is present a circular constriction. The superficial veins are prominent, especially towards the broad end of the sac, where are also seen the cut end of the cystic duct and the cystic lymph gland. This part of the gall-bladder looks and feels almost solid owing to the tumour within. The sac wall, which has a red velvety lining and is in general firm to the touch, is about ¼ in. thick, except

at the point of drainage, where there is an irregular dense thickening. Some 7·5 cm. from the orifice there is a thin projecting shelf corresponding to the constriction mentioned above; in part of its extent this is formed by all the components of the wall, the remainder being of mucosa alone.

On opening the region of the neck, a massive tumour is seen. This is a cauliflower-like growth, 3 cm. high, which is present as three main masses with numerous subsidiary and closely adjacent polyps; indeed, the proximal 5 cm. of the gall-bladder lining is almost entirely tumour-bearing. The main masses have a uniformly fleshy colour and appear almost solid; their surface, however, shows marked irregularity both gross and fine in type and on close examination they are seen to be essentially papilliform.
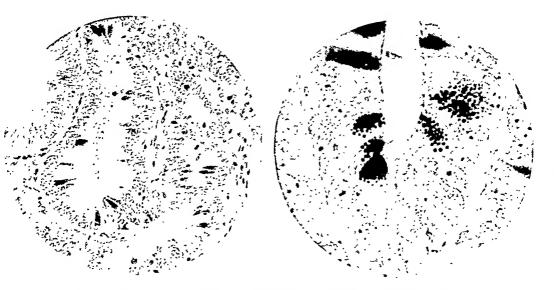
Several portions of the general gall-bladder wall were examined histologically. In all of these the serous coat is ill defined; the muscular coat likewise is poorly demarcated and throughout its breadth the muscular fibres are much interrupted by œdematous fibrous tissue. The blood-vessels show œdema of their walls and, in places, slight endarteritis. There are also throughout the wall many small localized areas of infiltration of lymphocytes, plasma cells, and some endothelioid cells; in a few of the larger of these areas the cells are mainly polymorphs, with an unusual concentration of eosinophils at the margin. At the internal surface the inflammatory cells form an almost complete boundary zone; in parts this is surmounted by gall-bladder epithelium. The infiltrated layer is composed almost entirely of plasma cells; there are also a few lymphocytes and an occasional polymorph, this latter type being seen especially in the prominent congested young capillaries of this zone. The epithelium is of the usual columnar

FIG. 437.—Inner wall of gall-bladder removed at second operation, showing at the upper end a large papilloma and at the lower end the thickened mass alongside the drainage opening. (× ½.)

form with basal nuclei of oval rather vesicular type. Crypt formation is present, but is of shallow type, the crypts nowhere extending more than a short way into the muscle coat; they are completely lined with epithelium. Toward the neck there is less evidence of inflammation, but crypts are also present in this situation.

Section of the thickened mass at the point of drainage shows a chronic inflammatory tissue of dense fibrous type with hyaline change both in the stroma and in the walls of a thrombosed vessel; lying among this fibrous tissue is a small amount of blood pigment. Covering the mass there is an almost intact sheet of

FIGS. 438, 439.—Photomicrographs showing the complex villous structure of the papilloma. *Fig.* 438, hæmalum and eosin. (× 7.) *Fig.* 439, hæmalum and eosin. (⁄ 35.)

FIGS. 440, 441.—Photomicrographs showing distribution and characters of the Paneth cells in the epithelium of the papilloma. *Fig.* 440, Gram's stain (modified) and carmalum. (× 250.) *Fig.* 441, phosphotungstic acid hæmatoxylin. (× 900.)

gall-bladder epithelium with slight crypt formation and an underlying zone of infiltration as described in the general sac wall.

The cystic duct shows a normal epithelium with mild chronic inflammation confined to the submucosa. In the cystic gland there is hyperplasia of the lymph follicles. The cystic artery shows hypertrophic nuclei in the muscle cells of the media and a slight fibrocellular intimal thickening.

The tumour itself presents the features of a complex papilloma (*Figs.* 438, 439). The stromal core is everywhere thin and shows only a few blood-vessels which, however, are markedly congested. Scattered irregularly throughout the stroma are areas of infiltration with inflammatory cells ; these are mainly lymphocytes, but polymorphs are seen nearer the base of the tumour and also occupying an intra-epithelial position in some of the outer fringes of the papilloma. Despite the apparently compact character of the tumour, section of the marginal area shows the attachment to be in the form of numerous tendril-like stalks. No suggestion of malignant invasion of the wall by tumour is seen in any of the sections examined, but among the stalks there are a few crypts lined by an epithelium of the same type as in the papilloma.

The epithelium of the papilloma is in general tall and columnar in type. The elongated nuclei form an irregular crowded layer on the basement membrane ; mitosis is occurring but is infrequent in proportion to the overcrowding of the cells. The cytoplasm of the cells is well stained and somewhat basophilic ; at the free edge it shows a striated border which is considerably more marked than in the epithelium of the general gall-bladder wall.

In the hæmalum and eosin sections of the tumour, many of the epithelial cells are seen to contain refractile eosinophilic granules ; these cells are easily distinguished under the usual high-power magnification of 360. The following staining reactions are noted for the granules :—

Reinke's neutral gentian	Purple
Bensley's orange G, acid fuchsin, and toluidin blue mixture	Fuchsin red
Heidenhain's iron hæmatoxylin	Black
Maximow's eosin-azur mixture	Red
Mann's eosin and methyl blue	Mainly red
Van Gieson's stain	Red
Malachite green and acridine red (*Fig.* 442) ..	Bright green
Mallory's phosphotungstic acid hæmatoxylin (*Fig.* 443)	Dark purple black
Gram's stain	Purple
Celestin blue, gallic acid eosin, and light green ..	Bright red
Celestin blue alone or with alcoholic chromotrope 2R	Unstained
Masson's silver method	Not impregnated

The granules are of various sizes ; in some cells they are uniformly small and the cell stretches as a narrow band of tiny granules from basement membrane to free edge ; in most, the inclusions are larger and the cells show a globular distal portion distended with granules ; in others the granules are of different sizes ; an occasional cell contains as few as four or five granules, but these are as large as 3 μ in diameter. Here and there the granules are seen in the process of extrusion and occasional clusters are apparent lying free.

The nucleus of the granular cell lies towards the basal part of the cell and shows no characteristic difference from the surrounding nuclei. None of the
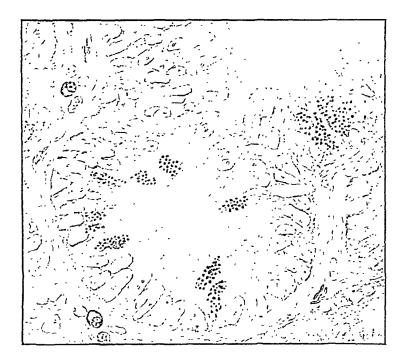
FIG. 442.—Projection drawing (A.C.L.) from papilloma showing selective staining of Paneth granules (granules and erythrocytes, bright green ; plasma cells, deep red). Malachite green and acridine red. (× c. 800.)
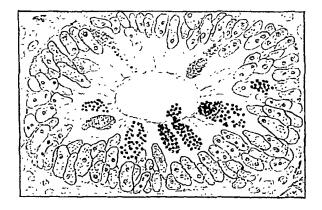
FIG. 443.—Projection drawing (A.C.L.) from papilloma showing varieties of distribution of Paneth granules, relation to goblet cells, discharge of granules, and intestinal type of free edge. Phosphotungstic acid hæmatoxylin and mucicarmine. (× c. 800.)

granule-containing cells are seen to be in mitosis. It is concluded from the shape of these cells and from the size, distribution, and colour reaction of the granules that they are Paneth cells. (*Figs.* 440–443.)

Also present in the epithelium are true goblet cells of the usual intestinal type; they are scarcely one quarter as numerous as the Paneth cells. The mucin gives a rather faint but characteristic coloration with mucicarmine, hæmatoxylin (of Delafield type), and celestin blue.

Neither Paneth nor goblet cells are present in the general wall except in those portions which lie between the roots of the papilloma. A very few cells of the tumour epithelium when stained with phosphotungstic acid hæmatoxylin followed by mucicarmine, or with Bensley's trichromic mixture, show Paneth granules in the deeper part with, towards the free edge, a transition to an almost homogeneous material giving the colour reaction for mucin. A still smaller number of cells shows the mucin-staining material deep to the granules.

After the use of Masson's method for sections, a very few cells are seen to have reduced the silver. These cells, which are all situated on the basement membrane, are small in size and do not appear to have any connection with the lumen; the silver-reducing granules which characterize them lie almost entirely in the infranuclear region. There seems no doubt that these are enterochromaffine cells (Kultschitzky, Ciaccio-Masson, ' yellow ', ' basogranular ' cells). No macro-granular leucocytes (Schollenleukocyten) are definitely identified.

This is a simple papilloma in the gall-bladder, covered by an epithelium which has the essential characters of intestinal epithelium, containing large numbers of Paneth cells, some goblet cells, and a few enterochromaffine cells.

Notes on Technique

With the exception of a loose fragment fixed in Zenker's solution (with 2 per cent acetic acid), the specimen was fixed in a Kaiserling's solution (pot. acetate 28 grm., chloral hydrate 27 grm., pot. nitrate 15 grm., formalin 150 c.c., water to 2000 c.c.).

Portions taken for histological examination were post-chromed by Kernohan's method[1] and after treatment with aqueous phenol solution[2] were brought through an ethyl-butyl alcohol series to butyl alcohol[3] and thence to paraffin. Of the stains mentioned, Reinke's neutral gentian was used as given under Bensley's neutral gentian in Carleton,[4] except that crystal violet was substituted for gentian violet (Conn[5]). Bensley's trichromic stain was used as given by Klein.[6] The phosphotungstic acid hæmatoxylin of Mallory was found particularly satisfactory as a stain for the granules, and a striking picture was seen after three hours' staining, the pre-treatment with permanganate being omitted. This form of staining, if followed by washing to reduce the red element of the hæmatoxylin, allows counterstaining although slowly with mucicarmine. Malachite green with acridine red is an easily used stain to show up the granules; this mixture, which Hitchcock and Ehrich[7] have proposed for the staining of plasma cells and Aschoff-body cells in tissues fixed by Zenker's fluid, has been found also to be very satisfactory for many other purposes, whatever the fixative, if the section is left for ten minutes in 1 per cent acetic acid, rinsed in water, and then stained as directed by the authors. With this stain the Paneth cells show bright green granules standing out against the soft pink of the cytoplasm; this affinity for the green is very marked, the granules retaining the stain even if the green be differentiated almost completely out of the nuclei.

The granules have been found to be Gram-positive, and an excellent picture is produced by Gram's stain following carmalum. Kirkpatrick's modification (unpublished) of the Gram-Weigert method for sections,[8] in which a sodium chloride solution replaces the Lugol's mixture, gives a very clear delineation of the granules, and appears, like phosphotungstic acid hæmatoxylin, to stain a higher percentage of the granules than the other stains used.

Some difficulty is experienced in comparing the results seen in different animals, since not only do different fixatives affect the staining of the granules and indeed also of the mucin, a point that will be further discussed below, but also the mucin of different animals may show different staining reactions and so make the recognition of the granules extremely difficult. This point was well brought out when carbol-thionin was used on Kaiserling-fixed mouse duodenum; here, with acetone dehydration, the mucin was pink and the Paneth granules dark blue; the same method when used on our tumour tissue showed the mucin retaining the blue stain and so failed entirely as a specific stain for the granules. Similarly with Kirkpatrick's stain the violet was almost completely removed from the mucin in the tumour tissue by aniline oil - xylol, but in formalin-fixed cat duodenum the mucin strongly resisted decolorization. Staining with celestin blue[2] for twenty minutes, followed by five minutes in fresh 1 per cent acetic acid, and then rapid dehydration, shows the nuclei blue, the mucin pink, and the granules unstained. Hamperl's[9] silver method did not seem to offer any advantage over the earlier method of Masson.[10] The most satisfactory staining of the granules seen with stains of the acid type was that produced by bichromate azo-eosin. This solution is prepared by mixing equal parts of 0·5 per cent aqueous solutions of azo-eosin and of potassium bichromate and filtering. Two minutes' staining is followed by differentiation in water and spirit.

THE SECRETORY ACTIVITY OF THE TUMOUR AND ITS RESULTS

RELATION TO MUCOCELE

Though the condition closely resembled that of mucocele in that the gall-bladder of a patient showing no jaundice was distended with a colourless fluid, it differed from mucocele in several respects. The fluid obtained when the gall-bladder was first opened was noted to be clear and watery, unlike the opalescent viscous content of a mucocele. Unfortunately no chemical analysis was made at this time. Further, the size of the gall-bladder exceeds that usually seen in mucocele. Judd and Castleton,[11] in 18,000 gall-bladders surgically removed, found only 35 with a long axis greater than 15 cm., and the largest which they record measured 20 cm. The long axis of the present gall-bladder after its removal measured 16·5 cm., and at the first operation when it contained 30 oz. of fluid, the gall-bladder must have been considerably larger; indeed, if proportional increase in its diameters is presumed, its long axis may be estimated to have measured 27 cm.

Nor did this gall-bladder behave during drainage in the manner of a mucocele. When a mucocele of the gall-bladder is drained without relief of the obstruction of the cystic duct, it is well known that the fluid drained diminishes rapidly in amount to a few cubic centimetres in twenty-four hours, and is of a viscid mucoid character. In this case the fluid output increased during the first eleven days to reach a peak at 154 oz., and during the last fourteen days was practically constant in amount at 65 oz. in twenty-four hours. Throughout the period of drainage the fluid maintained its watery character and showed a chloride content of about 0·8 per cent, a concentration which was considerably greater than that of the blood plasma (0·52 per cent NaCl).

Thus the condition was not one of mere mucocele but of distension by a watery fluid of high salt content presumably containing a small quantity of mucin. During the pre-operative stage this was evidently being produced at considerable pressure, while the amounts poured out after the institution of drainage show how vigorous was the underlying activity of the secreting surface.

SOURCE OF THE FLUID

The three possible sources of the fluid in the present case are the surviving gall-bladder epithelium, the areas of granulation tissue, and the epithelium of the tumour. In considering the first of these, we find that the only proved secretion of gall-bladder epithelium is that of mucin, most obvious in the condition of mucocele. In relation to sodium chloride and water the normal function of the gall-bladder is indeed absorption. Rous and McMaster[12] demonstrated that the gall-bladder concentrates the non-diffusible constituents of the bile at the expense of the diffusible without alteration of the osmotic pressure, which remains the same as that of the blood. This is effected by the almost complete removal from the bile in the gall-bladder of certain of the inorganic salts secreted by the liver, allowing the retention in the bile in greater concentration of bile salts and pigments, soaps, cholesterol, lecithin, and fats. Chabrol[13] similarly found that while the chlorine content of hepatic bile was 0·17 per cent, that of bile from the gall-bladder was only 0·005 per cent, a very marked reduction.

Even in a " white bile system " the chloride content of gall-bladder bile is relatively low. When obstruction of the common bile-duct occurs the retained bile is replaced by the colourless secretion of the bile-ducts and gall-bladder, constituting a " white bile system ". The establishment of such a system is delayed in the presence of a healthy gall-bladder, presumably on account of its continued concentrating activity (Rous and McMaster[14]). Chemical investigation by Sjöqvist[15] of the contents of a white bile system associated with carcinoma of the pancreas showed a lower content of inorganic salts in the gall-bladder than in the common bile-duct.

Ravdin and others,[16] while studying the absorption of chlorides from the bile-free gall-bladder of the dog, showed that under certain artificial conditions the gall-bladder may actually secrete water and chlorides. Following the experimental introduction of saline solution at different concentrations, the osmotic pressure of the solution approached that of the serum within a few hours. Where hypertonic solutions were used, chlorides were absorbed, while at the same time water was secreted until isotonicity was reached. In a number of such experiments the establishment of isotonicity was succeeded by the secretion by the gall-bladder of a fluid containing 0·55 to 0·58 per cent of sodium chloride at a rate of less than 1 c.c. per hour. This the authors presume to have been due to damage to the gall-bladder wall by the hypertonic solution. In these cases chlorides occurred in the drainage fluid in the same concentration as in the blood, and the amount of fluid secreted never approached, even relatively, the quantities shown in *Fig. 436.*

We know of no circumstances, clinical or experimental, in which the gall-bladder has been known to secrete fluid comparable in constitution or amount to that in the present case.

Granulation tissue frequently replaces portions of the gall-bladder epithelium in chronic inflammatory conditions. Cholecystostomy in these cases is never followed by prolonged drainage of large quantities of fluid. Nor does granulation tissue in other situations produce fluid of this character or in this quantity.

It is therefore held that the main source of the fluid in the present case was the epithelium of the tumour. The significance of this will be considered along with the cytology of the tumour.

NATURE AND IMPLICATIONS OF THE FLUID LOSS

The clinical picture of dehydration which appeared a few days after the institution of drainage of the gall-bladder led to a more critical interest in the amount and constituents of the fluid lost externally. The outstanding features, to which reference has already been made, were its large quantity and high chloride content. Two estimations of the sodium chloride content of the fluid gave values of 0·79 and 0·81 per cent, this latter figure being obtained during a period when in fact dehydration was clinically manifest, urinary chloride practically absent, and the blood-plasma chloride low (0·52 per cent). It may be taken, then, that the chloride content of the fluid was fairly constant at about 0·8 per cent, and therefore the output may be calculated to have reached 35 grm. in the 154 oz. of fluid drained on the eleventh day, and during the later stabilized period to have been about 15 grm. in the 65 oz. of fluid per twenty-four hours. The tumour epithelium appears to have excreted essentially sodium chloride and water.

Massive loss of fluid and chlorides from the upper alimentary tract is most commonly seen in acute intestinal obstruction, but may also occur following the marsupialization of a pancreatic cyst (Janes[17]). The relative amounts of the various electrolytes lost in this way vary with the source of the fluid, so that different modifications of the acid-base equilibrium may be produced. Thus alkalosis is a recognized accompaniment of acute high intestinal obstruction, while in the external drainage of pancreatic juice acidosis may occur (Dragstedt[18]). In the present case an estimation of the alkali-reserve during a period of dehydration gave a normal value, which suggests that there was no marked alteration in the acid-base equilibrium.

The vast outpouring of sodium chloride and water by this tumour is in keeping with the observations (McIver[19]) on isolated loops of jejunum, that the upper part of the small intestine pours out a fluid of high chloride content. There was in this case dehydration and salt-depletion comparable to that of intestinal obstruction, without, however, any causative abnormality of stomach or intestine. The rapidity with which this clinical condition arose from the loss of what we may take to be " jejunal secretion ", indicates the prominent part which may be played by the loss of intestinal secretion in the production of dehydration in intestinal obstruction. It also renders more explicable the occasional appearance of dehydration in the human subject prior to the onset of vomiting, and its constant occurrence in experimental obstruction in the rabbit, an animal where, through inability to vomit, large quantities of fluid accumulate in the stomach (Gamble and McIver[20]). In these cases we presume that the jejunum, like the stomach, continues to secrete a chloride-containing fluid which on account of the obstruction is functionally outwith the body, and no more available to that part of the bowel normally more absorptive than was the fluid drained to the exterior in the present case.

The prodigality of the tumour epithelium with chlorides is in marked contrast to the economy shown by the kidney. The tumour poured out chlorides continuously; the urine contained appreciable quantities only for a short time after each intravenous administration of saline. The state of the urinary chlorides, indeed, gave an earlier indication of chloride depletion than did the clinical condition of the patient. For this purpose the usual test-tube estimation with nitric acid and silver nitrate sufficed. Even during the periods when the clinical condition

resembled a severe intestinal obstruction, there was not the marked fall in urinary volume described in cases of intestinal obstruction (McIver[19]).   Despite the gross fluctuations in water balance, the continued efficiency of the kidneys is apparent from the normal urea content of the urine and the blood.

The most striking fact in the case is that this tumour, not 3 in. in diameter, concentrated sodium chloride from the blood plasma and poured it out at such a rate as to produce gross dehydration and chloride deficiency.

DISCUSSION ON THE INTESTINAL CELL TYPES IN THIS TUMOUR

IDENTIFICATION OF THE PANETH CELL

The unusual histological picture already described has led to an extensive cytological investigation in this case.   The literature on the Paneth cell is far from conclusive and almost entirely confined to studies on animals, so that the identification of the granular cells in this case necessitated some repetition of animal work to establish the validity of our technique.   We hope to show that despite the unique site, true Paneth cells and enterochromaffine cells are present in this tumour and that, in so far as they are cell-types independent of one another and of the goblet cell, their presence is proof of the intestinal character of the tumour.   The association in this case of Paneth cells with a profuse secretion will be considered as a possible clue to their little-known function.

The normal occurrence of Paneth cells has now been widely reported in the small intestine of vertebrates, but no record has been found of their presence in the gall-bladder.   They have been reported in man as occurring throughout the small intestine and also (Oppel[21] and Clara[22]) in Brunner's glands.   Patzelt[23] reports the finding in the human embryo of Paneth cells in those parts of the pancreatic and bile-ducts just adjacent to the ampulla of Vater.   They are present in small number in the human appendix and cæcum, but probably not beyond that.

To prove the identity of our granular cells with those generally called Paneth cells, there is unfortunately no specific method.   They, however, conform fully to the description given by Klein[6] and by Kull[24] and resemble the photographs in the latter's paper.   Tehver,[25] faced with the same difficulty in proving that certain granular cells present in the Brunner's gland of the horse were Paneth cells, quotes Clara's statement[26] that Paneth cells have no definite characteristic other than their granularity.   A further source of difficulty lies in the generally accepted fact that neither method of fixation nor type of staining reaction is capable of differentiating the granules of the Paneth cell from those of other granular cells such as the macrogranular leucocyte (Schollenleukocyte, Weill[27]) or the acidophil stage of the enterochromaffine cell.   The eosinophil polymorph may occur in considerable numbers in the connective tissue and even occasionally between the epithelial cells, while the form of degenerate plasma cell which has circular acidophil vacuoles (Russell bodies) in its cytoplasm may also be present to provide a further complication.   Of these different granular cells, the macrogranular leucocyte is the only one which is not an established type in the human intestine.

All the stains mentioned were tested on mouse jejunum, a site stated in the literature to be rich in Paneth cells.   These cells were readily demonstrated, and

their reactions with every stain proved similar to those in the cells in question, although there was more irregularity in staining than in the tumour. The same stains were tested on cat jejunum. No granular cells resembling Paneth cells were seen in the crypts, but at the level of the neck of the crypts numerous granular cells were found in the epithelium ; these cells are oval in shape and lie apposed to the basement membrane, not stretching out towards the lumen in the manner of Paneth cells ; they differ also from Paneth cells in the circular shape and dark staining of the nucleus, and in the larger size of their granules. The granules, however, except that they are not stained by carbol-thionin, show an exact similarity in staining reaction with those of the Paneth cells. There seems no doubt that these cells are macrogranular leucocytes (Schollenleukocyten).

At the foot of the crypts in the jejunum of the cat and also of a pigeon (*Columba livia*) an occasional goblet cell was seen in which the mucin was definitely granular and the outer or almost expressed granules showed a marked affinity for the green in the acridine red - malachite green mixture, while the deeper mucin stained brown as in the mucin cells in other parts. The other staining methods, of which phospho-tungstic acid hæmatoxylin seems the most reliable, confirmed the finding of Kull and others that there are no Paneth cells in the jejunum of the cat, and the finding of Baecker[28] that they are absent also from *Columba livia*. Observations on human operation material, which will be discussed under the heading of the occurrence of Paneth cells, further confirmed our use of the stains mentioned in the literature and also the validity and excellence of the three additional methods proposed as stains for Paneth granules.

The basis on which we can presume our cells to be Paneth cells lies in their shape and situation, and in the morphology, staining reactions and disposition of the granules.

Recognizable stages in the cycle of the Paneth cell have been suggested by Mols,[29] but, as he himself pointed out, the picture varies with the fixative used, a fact which has been emphasized by almost all workers on this subject. On comparing the effect of a series of fixatives (Hollande, formol-corrosive, Regaud, formalin, Kaiserling) on mouse jejunum, it is found that Kaiserling is an excellent preservative of the granules. Actually in the tumour tissue the percentage of granules staining poorly with phosphotungstic acid hæmatoxylin is considerably lower than in the correspondingly fixed mouse tissue. (The mouse was killed at mid-day without having received food that day.) Such granules in the tumour tissue as stain weakly appear to occupy no special position or relation in the cell. A further source of difficulty in justifying any conclusions based on the staining properties of the granules lies in the fact that some of the stains definitely colour a higher percentage of the granules. In view of these difficulties and the uncertainty in the literature, there seems no possibility of definitely correlating the histological picture with any stage of secretory activity on the part of the Paneth cells.

The normal position of the Paneth cell is strongly in favour of its being secretory. In man it occurs mainly in the small intestine, where a large and important secretion is poured into the lumen ; its presence in very small numbers in the human cæcum is not a counter-argument, since a small amount of secretion is produced in the large intestine.[30] Its situation in the crypts and not on the villi is likewise in favour of an active or secretory function, as is the often observed discharge of the granules. A further argument is found in the present case : the

large amount of fluid has already been shown to be the product of the tumour epithelium, and so either the Paneth cells or the non-granular cells, whether or not they are different stages of the same cell, must be the source of this fluid.

THE PANETH CELL AND THE GOBLET CELL

The relationship of the Paneth cell to the other types of normal intestinal cell has been deduced mainly from observations on the lower animals. Clara,[26] from work on avian material, considers that it is normally a type *sui generis*, and many workers concur in this view. Bizzozero[31] considered the Paneth cell a young mucin cell, while Kull,[24] supported by Chuma,[32] considers that it is a regressing mucin cell. Our findings certainly suggest a possible relationship between the goblet and the Paneth cell, in so far as we have found in different portions of the same cell the colour reaction for mucin, and also typically stained Paneth granules. This transitional type is well shown in the sections stained by phosphotungstic acid hæmatoxylin and mucicarmine. Bizzozero considered that in the cycle, the Paneth granules become smaller and then a mucin reaction develops at the free end of the cell. In most of our transitional cells the appearance conforms to his illustrations but in a few the relative disposition of mucin and Paneth granules is reversed.

Clara,[26] in stating that the Paneth cell is a type *sui generis*, is apparently fully cognisant of the mucin-like staining in some Paneth cells ; he points out that mucin-stains are not entirely specific and states that variations in this can depend on the fixative used. This fact was well seen when staining mouse intestine by Kirkpatrick's stain ; tissue fixed in Kaiserling allowed easy decolorization of the mucin, and so was satisfactory for observing the Paneth cells, but after fixation in formol-corrosive, Hollande's or Regaud's fluid, the mucin held the violet almost as strongly as does cat mucin. Baecker[28] more recently has again pointed out the basic staining of Paneth granules after picric acid fixation, a finding which is explained in some measure by Boerner-Patzelt,[33] through a study of the iso-electric point of the Paneth granules after different fixatives. Thus, in a critical examination of the transitional type of cell, both fixative and stain demand scrutiny. From work on mouse tissue it appears that formalin solution (sodium chloride 10 grm., sodium sulphate 30 grm., formalin 200 c.c., water 800 c.c.) or Kaiserling's solution is not only a better fixer of the granules than is formol-corrosive, Hollande's or Regaud's fluid, but is also a better mordant, in that the granules stain more uniformly. On the tumour tissue Kaiserling's solution likewise showed both these advantages over Zenker's fluid. It may therefore be justifiably presumed that the gall-bladder was fixed unwittingly in the most suitable fixative for Paneth granules. The phosphotungstic acid hæmatoxylin solution (naturally ripened) after three hours' staining showed the granules of a deep purple colour, and with subsequent treatment with water and spirit there was little or no evidence of any staining of the mucin. For optimum although slower staining the sections should be pre-treated with a reducing agent such as potassium metabisulphite. Southgate's mucicarmine was used as the stain for mucin, and from staining of animal intestine it would appear that the phosphotungstic acid hæmatoxylin beforehand does not deviate the specificity of this stain. It is therefore held that if cells exist which contain both mucin and Paneth granules, then the technique outlined above is optimal for their exhibition. The fact remains, however, that mucicarmine also stains cartilage and tissue

which has undergone myxomatous degeneration, and so a substance may be present in Paneth cells which stains red and is yet not mucin.

Also against a relationship between the two cell types is the observation that various stages of development up to discharge of the cell contents are seen in both the Paneth and the mucin cell; further, the rarity of the transitional type is remarkable if the numerous Paneth cells in this tissue are really related to the far from infrequent goblet cells. The relationship between these two cell types remains an open question.

Goblet cells do not occur, according to Maximow,[30] in the normal human gall-bladder. They have, however, been reported in the extrahepatic biliary ducts of man, mainly in "the intestinal portion of the ductus choledochus" (Macklin[34]), and are present in the gall-bladder of some animals (Macklin).

Whatever the relationship between goblet cell and Paneth cell in the normal intestine or even in this tumour, the actual presence of goblets may be considered at least confirmatory of the possibility which the Paneth cells suggest, that the epithelium of the tumour is truly intestinal in type.

THE PANETH CELL AND THE ENTEROCHROMAFFINE CELL

The silver-reducing cells in the tumour have the situation, the appearance, and that type and disposition of their granules which justify our recognizing them as enterochromaffine cells. The presence of these cells is of interest in view of the existing controversy as to their origin.

Cells of this type have been reported by Tehver[35] in the gall-bladder of the cow, but no record has been found of their existence in the human gall-bladder (quoted Hanser[36]), although Patzelt[23] has found them in those parts of the pancreatic and biliary ducts just adjacent to the ampulla of Vater in the human embryo, where he also described Paneth cells. All our enterochromaffine cells show a very definite localization of the granules in the basal part of the cell, a disposition which, according to Hamperl,[9] is very marked in the normal human duodenum.

The number of silver positive cells seen in the tumour sections is small, but, as Masson[10] points out, the silver reaction is capricious when applied to sections. According to Macklin, the enterochromaffine cell granules degenerate more rapidly than those of the Paneth cell and so the ratio of the two types as seen is possibly not a true index. The tissue, however, was in fixative solution within half an hour of removal, and Hamperl[9] estimates that it is four or five hours before the granules lose their silver-reducing power.

Enterochromaffine cells are few, according to Tang,[37] in those animals in which Paneth cells are numerous, as in the squirrel; the opposite condition also holds good, as is typically seen in the pig. Whether this numerical relationship, which is accepted by other authors, signifies any functional relationship is a very open question. Kull[38] is quite definite that no possible relationship can exist, basing his argument on the findings in those animals in which Paneth cells are very few or absent. Cordier's work,[39] in which under the influence of pilocarpine both enterochromaffine and Paneth cells are seen to lose their granules, suggests that they are both entodermal secretory cells, but Macklin[34] some years later still considered that there was no real evidence that the enterochromaffine cells are in any way concerned with digestion or absorption. The evidence from the literature

does not seem to show much in favour of a relationship between the Paneth cell and the enterochromaffine cell, nor does it give any satisfactory proof of an entodermal origin for the enterochromaffine cell.

Normally the enterochromaffine cell is confined in the human subject to the alimentary tract proper and has never been recorded in the gall-bladder; whichever view is held as to the origin of this cell, its occurrence in the tumour epithelium but not in the general gall-bladder wall is significant evidence of the intestinal nature of the tumour.

We have therefore in this gall-bladder tumour three intestinal cell-types capable of histological identification, two of which have never been reported in the human gall-bladder.

THE PANETH CELL IN PATHOLOGICAL CONDITIONS

The relationship of this cell to pathological processes is apparently little known, but the scanty evidence from which it has been assumed by some that Paneth cells are increased near a focus of irritation must now be examined. The occurrence of Paneth cells in the intestinal islets of the stomach will be discussed later.

Schmidt,[40] who states that Paneth cells are practically absent from the large intestine, found them in three cases. Two of these were of simple polyp with Paneth cells in the epithelium of the growth itself. The third case was of carcinoma, and Paneth cells were noted in the otherwise apparently normal epithelium immediately adjacent to the malignant transition. Unfortunately there is no note of the part of the large intestine involved. Eklöf[41] reports the presence of numerous Paneth cells in the neighbourhood of a carcinoma in the transverse colon, and this would appear to be the one substantiated case in which Paneth cells have been recorded in the actual epithelium of the large intestine distal to the cæcum in the human adult. His only other observation was made on large intestine from an operation for strangulated hernia, but in this he found no Paneth cells. The implication drawn from this work has been that Paneth cells are increased in the neighbourhood of a focus of irritation. With a view to testing the truth of this, some pathological and normal operation material was examined after staining by phosphotungstic acid hæmatoxylin. The sites and results are seen in *Table I*.

From *Table I* it will be seen that Paneth cells were found in large numbers, actually two to seven per crypt and in five out of six crypts, in the small intestine and in a perfectly healthy Meckel's diverticulum. An occasional Paneth cell was seen in the cæcum and in the appendices examined, but none in the remainder of the adult large intestine. The available portions of normal epithelium unfortunately do not make a complete control, but from one of the resections for carcinoma of the cæcum (*Case 4*), ileal mucosa was available up to 15 cm. from the still patent valve, and cæcal mucosa to 5 cm. distal to the tumour. In a comparison of the cæcal portions there was a very slight increase in the number of Paneth cells toward the growth; since the general view is that Paneth cells occur in the cæcum and not in the remainder of the colon, this gradation may be taken as normal. In examination of the 15 cm. of ileal mucosa, there appeared to be no variation in the number of Paneth cells except in the $\frac{1}{2}$ cm. immediately adjacent to the malignant change where Paneth cells actually were fewer. This diminution in the boundary zone was also seen in *Case 5*. In no case were Paneth cells or any cells resembling them

seen among those frankly carcinomatous, although Schmidt[10] quotes Saltykow[42] as finding Paneth cells in a few alveoli of an adenocarcinoma of the stomach.

Of the rectal papilomata from the child, one showed a single but quite definite Paneth cell (*Case* 18); the other (*Case* 19) showed none, but in this case the surrounding mucosa showed an interesting appearance. The epithelium, differing markedly from the tumour cells which are almost entirely chief cells, consists of the usual goblet cells, but in the deeper parts of the mucosa the crypts are continuous with glands of the 'pyloric' type. These are morphologically similar to

Table I.—SITE OF PANETH CELLS IN NINETEEN CASES

CASE	SITE	PANETH CELLS	CASE	SITE	PANETH CELLS
1	Normal jejunum ..	+++	10	Splenic flexure near carcinoma	—
2	Epithelium near infected diverticulum	+++	11	Splenic flexure near carcinoma	—
3	Ileum near sarcomatous ulceration	+++	12	Sigmoid colon near carcinoma	—
4	Ileum 15 cm. from carcinoma at valve	+++	13	Sigmoid colon near carcinoma	—
5	Ileum 8 cm. from carcinoma at valve	+++	14	Normal colon, colostomy	—
4	Ileum adjacent to carcinoma	+	15	Normal colon, colostomy	—
5	Ileum adjacent to carcinoma	+	16	Rectum near carcinoma	—
6	Meckel's diverticulum	+++	17	Rectum near carcinoma	—
7	Inflamed appendix	+	18	Papilloma of rectum (child)	+
8	Inflamed appendix	+	18	Adjacent epithelium	—
9	Inflamed appendix	+	19	Papilloma of rectum (child)	—
4	Cæcum near carcinoma	+	19	Adjacent epithelium	++
5	Cæcum near carcinoma	+			

the type seen in the deeper parts of the Aschoff-Rokitansky sinuses (Nicholson[43]) and are likewise negative to mucicarmine (formalin fixation). In the depths of the crypts, whether ending normally or in continuity with the 'pyloric' glands, there are numerous Paneth cells in the epithelium. An occasional Paneth cell is seen among the clear cells at the region of transition from goblet cells to clear cells.

Comparison with animal tissues is of little value as a guide to the normal condition in the human since the distribution varies so greatly. Trautmann[44] finds the condition in the horse and ass to be similar to that accepted for man,

whereas Hamperl[45] finds that in the mole and the bat Paneth cells are present in the large intestine almost to the anus.

It seems reasonable to conclude that in the human adult Paneth cells are numerous in the small intestine, scanty in the appendix and cæcum, and absent from the remainder of the large intestine. *There seems no reason for believing that a focus of irritation in any part of the adult intestine will lead to an increase of Paneth cells.*

HETEROTOPIA OR METAPLASIA ?

Having stated our belief that this tumour is formed of intestinal epithelium, we are now faced with the problem of how this arose in the gall-bladder. The process of metaplasia has been so often invoked to explain the intestinal islets in the stomach that its possible application to our case demands examination. We hope to show, however, that the specialized character of the cells present makes heterotopic misplacement the only acceptable solution.

Metaplasia " occurs when a differentiated tissue loses its characters and assumes those of another differentiated tissue."[46] The transition is generally towards a more protective form, and though this may be to a moderately specialized type as seen in the evolution of goblet cells from the epithelium of the extroverted urinary bladder, the usual association with mechanical or inflammatory irritation makes it understandable that there occurs no high degree of morphological or functional evolution.

In the heterotopic islands believed to be due to a dislocation of tissue during the period of development, a visibly complete perfection may be seen, and the peptic ulceration produced near gastric islets in a Meckel's diverticulum is one of the proofs that these areas may have a function corresponding to their appearance.

Metaplasia as usually seen in the gall-bladder shows an epithelial change in association with stone to the squamous form, or the appearance in the chronically inflamed viscus of Aschoff-Rokitansky sinuses with, in their deeper parts, areas of cells resembling ' pyloric ' glands.[43] Heterotopia in the gall-bladder has been reported by von Hedry,[47] who describes a case of accessory pancreas in the wall of the gall-bladder, while adenomyomata have been recorded in the wall, which, in the complete absence of signs of inflammation, have been considered as ' hamartomata '.[48] Egyedi[49] has recently described a papilloma of gall-bladder in which the epithelium was of gastric type, but no record has been found in the literature of heterotopic intestinal epithelium in the gall-bladder.

The commonest form of abnormally situated intestinal epithelium is that seen as islets in the stomach. Chuma[32] found areas of intestinal epithelium in the stomach of 15 of a series of 73 unselected autopsy cases. Paneth cells were present in this intestinal epithelium in 4 of these cases. In his observations on operation material, he noted *intestinal islands in the stomach of 28 (70 per cent) out of 40 cases* ; in all of these there were Paneth cells. These islands were in each case associated with or near a lesion, ulcer, cancer, or chronic gastritis. According to Chuma, who reviews the German literature on this subject, intestinal epithelium is never found in a normal stomach. Borrmann[48] later supports this view, and goes so far as to say that the intestinal islets occurring in the stomach of older adults must be considered as always due to a pathological condition of the viscus. Moszkowicz[50] explains the occurrence of the islets on the basis of differentiation

of an indifferent epithelium growing up in an irritated area, and uses for this the term ' indirect metaplasia '. Clar,[51] on the other hand, brings forward evidence from study of fœtal stomachs and of those parts of gastric resections well away from the lesion, in no case chronic gastritis, all of which goes to suggest that these islets are congenital displacements. Hurst and Stewart[52] also report the presence of intestinal islets in otherwise normal stomachs. The nature of the process leading to the presence of intestinal islets containing Paneth cells in the stomach is therefore not yet conclusively defined.

If the view were correct that these islets are due to metaplastic change, then the type of epithelium in the islet, however closely it resembled that of the small intestine, would require to be considered a de-differentiated form of gastric epithelium. There is no doubt that Paneth cells occur very commonly in these islets and would therefore have to be placed in the category of the less specialized alimentary types; they could then be considered a possible appearance in the debasement of any specialized alimentary epithelium, including that of the gall-bladder. We have attempted, on the other hand, to show that the Paneth cell is a specific cell-type structurally and functionally, which is not increased in the alimentary tract or produced in the gall-bladder in response to irritation. We therefore consider the presence of Paneth cells to be strong evidence in favour of the heterotopic nature of the present tumour.

The goblet cell lends no definite help to the argument. This type is present in our tumour and in the intestinal islets of the stomach, whereas normally it is not found in either gall-bladder or stomach. Thus it would seem to bear the same relationship to the question as does the Paneth cell. The frequency, however, with which goblet cells appear in the chronically inflamed gall-bladder without the appearance of other intestinal forms, suggests very definitely that they arise here by a process of metaplasia. This being so, we are unable to utilize their presence in our tumour as evidence that the epithelium is of fully formed intestinal type, even though this may well be the true explanation of their presence.

The finding in our tumour of enterochromaffine cells is of particular interest since it is a type which, so far as we know, has never been found in the human gall-bladder. There seems no doubt that this is a specialized cell, and, though its presence here is surprising if one accepts the hypothesis that the enterochromaffine cell has its origin outwith the entoderm, the finding of this cell definitely favours the view that this epithelium is not the product of metaplastic change.

It is therefore concluded that the epithelium of this tumour is truly intestinal, and sufficiently specialized in morphology and function to be explicable only on the view that the tumour arose in an area of heterotopic epithelium.

PAPILLOMA OF THE GALL-BLADDER: REVIEW OF PUBLISHED CASES

The statement that papilloma of the gall-bladder is a rare lesion introduces the subject in most of the standard works of pathology and surgery. A study of the literature has suggested that, even in some of the cases most frequently quoted, the diagnosis has been too readily accepted.

Much confusion has arisen within the last twenty years through the application of the term ' papilloma ' to lesions which many are unable to accept as in any true

Table II.—Cases Reported as ' Papilloma ' of the Gall-bladder

Author and Date	Features	Suggested Diagnosis
Heschl,[58] 1852	Localized polypoid fat-laden projections ; stone present ; character of probable secondaries in liver not confirmed microscopically	Carcinoma
Klob,[59] 1856	Two cases. Localized polypoid projections ; inflammation ; stone present	—
Rokitansky,[60] 1861 ..	Circumscribed polypoid lesion	—
Mettenheimer,[61] 1871 ..	Fat-laden papillæ ; bile in gall-bladder ; no stones	Cholesterosis
Schüppel,[62] 1880 ..	Small gall-bladder filled by papillary mass attached over a wide base (' myxopapilloma ') ; no bile in gall-bladder ; no stones	Papilloma
Birch-Hirschfeld[63] 1895 (?)	Circumscribed polypoid lesion	—
Ringel,[64] 1899	' Multiple papillary fibromata ' considered to be possibly early carcinoma, but patient was well 4 years later	Cholecystitis polyposa
Hansson,[65] 1905 ..	Enlarged gall-bladder filled by pus, stones, and a degenerate papillary mass the size of a fist	Papilloma
Pels-Leusden,[66] 1906 ..	Cholecystostomy ; generalized papillary formation ; high cylindrical epithelium. Two years later similar growth at mouth of fistula. Death three years thereafter from phthisis ; stone in common bile-duct ; no secondary tumours	Papilloma
Sand and Mayer,[67] 1910	Mucocele relieved by removal of enlarged cystic gland ; no stone ; generalized papillary formation (papillæ 2 mm. long) ; goblet cells present. "An exaggeration of the normal delicate villi "	Cholecystitis polyposa
Dominici,[68] 1911 ..	Mucocele ; generalized papillary growth (papillæ 5 mm. long) ; goblet cells present	Cholecystitis polyposa
Schoenlank,[69] 1914 ..	Enlarged gall-bladder with papillary projections; epithelium many layered ; bile-coloured mucin in gall-bladder; stone previously passed. Second operation—papillary carcinoma in left lobe of liver. Squamous epithelium alongside an area of ulceration in the gall-bladder	Carcinoma
Kaufmann,[70] 1922 ..	Three cases. Each had several small tumours ; no detail of size ; no histology ; accepts Sand and Mayer's case and this lesion is therefore presumably comparable	Cholecystitis polyposa

Table II.—CASES REPORTED AS 'PAPILLOMA' OF THE GALL-BLADDER, *continued*

AUTHOR AND DATE	FEATURES	SUGGESTED DIAGNOSIS
Landsberg and Zaorski,[71] 1923	Cholecystectomy for chronic cholecystitis, gall-bladder contained bile and, in the fundus, a stalked papilloma; no histology in abstract	? Papilloma
Abell,[72] 1923	Two cases. Multiple papillary outgrowths One case. Operation for acute cholecystitis; gall-bladder filled with villous growth considered malignant (no histology); cholecystostomy. Three years later, operation for common bile-duct obstruction, no sign of gall-bladder; non-malignant papillary adenoma in common bile-duct, thought to be possibly a transplant from the original growth	Cholecystitis polyposa Papilloma
Risak,[73] 1927 . ..	Polypoid adenoma lying free in gall-bladder, size of hen's egg; no stone; too necrotic for histological study	? Polypoid adenoma
*U C H,[71] 1929	Annular villous papillary growth 1·5 × 0·5 in.; single stone; delicate fibrous tissue processes with myxomatous change covered with a layer of columnar epithelium of gall-bladder type; goblet cells present; no Paneth cells	Papilloma
Vecchi,[70] 1929 .	Papillary tumour the size of a hen's egg; histologically complex villous papilloma with tall columnar epithelium, single layer with 'border' at free edge. No goblet cells in tumour; gall-bladder contained bile but no stones	Papilloma
Henry,[76] 1933	Sessile growth, 2·5 cm wide and several smaller isolated growths; also one in cystic duct and one in common bile-duct Histologically—simple papilloma	Papilloma
Egyedi,[19] 1934 ..	Operation for chronic cholecystitis; mucocele with single stone and tumour at neck. Histologically—papilloma consisting of gastric epithelium including chief and parietal cells	Papilloma of heterotopic epithelium
*R C S. Edin (unpublished) .	Obstructive jaundice with colic; cholecystectomy; numerous small stones in cystic duct; gall-bladder contained soft papillomatous material (a), and had a thick irregular wall (b). Histologically. (a) Somewhat degenerate villous papilloma; no apparent Paneth cells (b) Carcinoma	Carcinoma

sense neoplastic. Thus Mayo[53] states that in papillomatous cholecystitis the 'papillomas' vary from twice to five or six times the length of normal villi and are laden with a fatty substance responsible for their yellowish appearance; MacCarty[54] goes further in saying that these papillomas are histologically identical with the villi in the strawberry gall-bladder, being merely larger and branched. These writers are obviously describing the familiar cholesterol polyp, and, as Graham[55] has suggested, a clear differentiation should be made between this condition and true papilloma. Phillips,[56] who with Mayo applies the term 'papilloma' to the cholesterol polyp, describes in addition a sessile papilloma due to infection; his account of the gross and microscopic appearances of this and the associated conditions suggests only the proliferation commonly seen in chronic cholecystitis. Nothing is gained by attributing to this lesion a name which implies that it is essentially neoplastic, and it would seem preferable to use the term 'cholecystitis polyposa' or, as suggested by King and MacCallum,[57] 'cholecystitis glandularis proliferans.'

The small pedunculated growths sometimes described as papillomata, but histologically devoid of villous formation and containing a high proportion of connective tissue, are probably to be looked upon as adenomata comparable to those occurring within the wall.

A further source of confusion in nomenclature occurs in the earlier cases in the German literature, where Heschl[58] and Klob[59] describe under the title of 'Zottenkrebs' what they themselves considered to be simple lesions.

The cases shown in *Table II* have been published or quoted as papillomata of the gall-bladder.

The classification of these cases has been rendered difficult by the lack of available detail, particularly in the earlier publications. On these grounds we do not venture to place in any definite category the cases of Klob, Rokitansky, Birch-Hirschfeld, and Landsberg and Zaorski. Mettenheimer's case we consider to have been one of cholesterosis with cholesterol polyp.

In the cases of Ringel, Sand and Mayer, Dominici, Kaufmann, and Abell (first two cases), the lesion was multiple or generalized, the outgrowths were small, and evidence of cholecystitis was present, though sometimes only in the form of stones or goblet cells. Here we consider the diagnosis to have been cholecystitis polyposa. Risak's case was probably one of polypoid adenoma.

The cases of Heschl, Schoenlank, and R.C.S. Edin. were definitely malignant. The papilloma of heterotopic epithelium described by Egyedi has already been mentioned along with our own comparable tumour.

The remaining cases, those of Schüppel, Hansson, Pels-Leusden, Abell (third case), U.C.H., Vecchi, and Henry, were, as far as we can estimate from the descriptions, discrete villous growths of considerable size projecting from the mucosa of the gall-bladder. The presence of subsidiary growths on adjacent portions of the gall-bladder wall, in the cystic duct, in the common bile-duct, or in a post-operative fistula, seems quite in keeping with a diagnosis of papilloma. Histological description, where available, was of a simple outgrowth of gall-bladder epithelium with a thin much-branched stromal core. In agreeing with Hanser[36] that the differentiation between papilloma and chronic proliferative cholecystitis is usually difficult, and while admitting that the inadequacy of description of many recorded cases makes retrospective classification insecure, we yet feel

that the cases in this last group do justify their classification as true papillomata of the gall-bladder.

Of the seven cases noted, three show simple transplantation, which, along with their villous structure, recalls the papillomata occurring within the urinary system. In the two recent malignant cases already mentioned, a comparatively simple villous papilloma was associated with adenocarcinoma of the gall-bladder wall. In Schoenlank's case the epithelium of the papillomatous portion was in part two-layered, but the appearances were virtually those of a benign tumour except at the base, where gradual transition was seen to frank malignancy with infiltration. In the R.C.S. Edin. case the available parts of the papillomatous portion show a hyperplastic but not definitely malignant epithelium. At the base of the tumour there is obvious carcinoma. From the description in Schoenlank's paper and the appearances in the R.C.S. Edin. case it seems reasonable to compare these tumours, as Illingworth[77] has recently done, with those villous papillomata of the urinary system which show so-called ' malignant transformation '.

Thus the cases accepted as papillomata of the gall-bladder fall naturally into three groups : (1) Simple villous papilloma ; (2) Simple villous papilloma with transplantation ; (3) Villous papilloma with ' malignant transformation '. It is noteworthy that this classification of the papillary tumours of the gall-bladder is identical with that frequently employed in the description of the corresponding lesions in the urinary system. The inter-relationship of these three groups is no further elucidated by our study, but the underlying connection would seem on histological grounds to be the same in the two situations.

Apart from the case of Egyedi, the epithelium of all the tumours found has been described or presumed to be of gall-bladder type. In no case has a tumour of intestinal epithelium been described. The only variation noted has been the presence of occasional goblet cells in the epithelium of the tumour in the U.C.H. case, but, as in the chronically inflamed gall-bladder, these occur merely as isolated units in an otherwise typical gall-bladder epithelium.

SUMMARY

An unusually distended gall-bladder causing no symptoms other than those due to its size was surgically drained. Thereafter surprisingly large volumes of fluid poured out from the wound. The fluid proved to be sodium chloride and water, at a concentration considerably higher than that of the blood plasma. Dehydration and chloride depletion resulted within five days and were successfully treated by intravenous administration of saline. The continued outpouring of fluid, which during one period of twenty-four hours reached $7\frac{3}{4}$ pints, necessitated the repetition of this treatment at intervals of five or six days throughout the thirty-four days of drainage.

The gall-bladder was then removed and found to contain a large papilloma. Histological examination showed the epithelium of this tumour to resemble that of the small intestine, with Paneth cells, enterochromaffine cells, and goblet cells. The source of the fluid is considered to be this intestinal epithelium, and the question is raised of the possible part played by intestinal secretion in the dehydration and chloride depletion of acute high intestinal obstruction. Estimation of the

urinary chlorides is advocated as providing an early indication of chloride depletion in comparable cases.

Histological investigation of the cell types in the tumour led to the conclusion that the Paneth cell, the enterochromaffine cell, and the goblet cell are independent types and that the presence of the first two, which have never been previously reported in the gall-bladder, proves that the epithelium is truly intestinal in character.

The specialized nature of the cells in this papilloma is held to show that the tumour arose in an area of heterotopic intestinal epithelium. A brief critical analysis is given of cases previously published as papilloma of the gall-bladder, including one papilloma of heterotopic gastric epithelium.

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THE TREATMENT OF ACUTE INTRAMAMMARY ABSCESS, BY INCISION AND BY ASPIRATION

By R. J. V. BATTLE AND G. N. BAILEY

SURGICAL REGISTRARS, ST. THOMAS'S HOSPITAL

AN account is here given of acute intramammary abscess with particular reference to treatment, and the statements we make are founded partly on the literature and partly on our own observations.   We have recently been in the position to observe every case of breast abscess treated at St. Thomas's Hospital over a period of about a year.   It has been possible to collect 71 cases, and careful records have been kept of each case.   Some of these patients were treated in the Out-patient Department, but those that failed to improve, and those in which suppuration supervened during the puerperium, were admitted to the Septic Block, where a certain number of beds were always available.

ETIOLOGY

It is not unusual to find suppuration in the non-lactating breast.   In a series of 102 cases, Bryant[11] (quoted by Sampson Handley) found an incidence of 20·5 per cent in cases that were neither pregnant nor lactating.   In our own series there were 11 cases, giving a percentage incidence of 15·5.

The abscess occurring in the non-lactating breast is of little clinical importance, apart from its occasional association with carcinoma.   The responsible organism appears to be the *Sta. aureus*, the path of entry being either from the nipple or from the blood-stream.   There appears to be no direct evidence in favour of either, as in our own series the nipple appeared to be perfectly normal and there was no evidence of septic foci elsewhere in the body.   As in most pyogenic infections, a lowered general condition, resulting probably from social conditions, appeared to be the underlying factor.   However, the prognosis in these non-lactating cases is good.

The abscess occurring during lactation presents a different picture.   The organism concerned appears to be either a *Sta. aureus* or a streptococcus.   The latter we believe to be very rare in breast abscess without secondary infection.   In no case of our series in which the pus was cultured was a streptococcus grown.   We therefore find ourselves in agreement with both Benians[1] and Moon and Gilbert,[19] in considering the streptococcus to be rarely a causative organism.   The organisms are present in the milk from normal breasts,[12] and in children's mouths.[13]   The actual portal of entry is debatable.   Benians has gone so far as to distinguish between two types of abscess : (1) That in which entrance is effected by strepto-cocci via cracks in the nipple ; and (2) That in which staphylococci find access to the breast by means of the ducts.   Hamilton Bailey[3] has confirmed this distinction.

The presence of cracked and sore nipples undoubtedly plays an important part in the etiology.   Ehrlich[5] found 24 per cent of cracks on macroscopical examination

of 84 cases. Kehrer[4] considered that of all cases of cracked nipple, 25 per cent developed mastitis. In 60 consecutive lactating breasts in which infection had supervened, we found 17 cases with a definite history of cracks and a further 19 cases with painful or 'sore' nipples. This gives 36 cases with a history of nipple trouble, an incidence of 60 per cent in all.

Sudden weaning or death of the infant, with its attendant breast engorgement, appeared to be a factor in 10 per cent of our cases.

Pain is the outstanding clinical feature of a cracked nipple. Owing to pain the mother cannot tolerate prolonged feeding on the breast, and unless the condition is bilateral, will prefer to feed the infant on the other side. In consequence of this the affected breast remains relatively engorged.

We believe that the essential action of a cracked nipple lies in the engorgement it produces and not in its action as a path of entry for organisms. It follows from this that the treatment of any nipple crack becomes of the highest prophylactic importance, a point already emphasized in the literature.[2] (In a recent paper the importance of nipple trouble has been discountenanced.[19])

PROPHYLACTIC TREATMENT

1. Before Engorgement.—There is no need to mention the steps to be taken in maintaining the integrity of the nipple, for these are repeated and emphasized in every text-book on infant feeding ; but one cannot help being struck very forcibly by the utter disregard of ordinary principles that should be employed once a nipple has actually become cracked or sore. These principles should be :—

a. Scrupulous cleanliness, without which all other treatment is surely useless.

b. The employment of hardening material, in the nature of Friar's balsam and perchloride of mercury.

c. The use of a shield for protection of the nipple at the first evidence of soreness, without awaiting the presence of a macroscopic lesion.

d. The use of a breast pump. This instrument is absolutely invaluable for use on the affected side, even where a shield is already in use, to make certain that the breast is completely emptied after feeding. The breast pump is condemned by some, since they consider that suction merely increases the output from the affected breast and thus produces the very engorgement to be avoided. This is a fallacious argument. Firstly, the breast pump is less stimulating than the normal direct feeding, and, secondly, it is always capable of draining any increased output for which it may have been responsible.

e. Where a shield fails to relieve pain, no further time should be wasted in direct feeding on the breast concerned. At the best simple engorgement will result. There should be no hesitation in removing the infant from the side in question and feeding it indirectly, the breast being completely evacuated with the breast pump, and the milk being administered by means of a bottle.

When the nipple has settled down these steps mentioned above are reversed until the baby is feeding directly on the unprotected nipple without the production of pain and engorgement.

2. After Engorgement.—Engorgement of the breast appears to be of two distinct types :—

a. A diffuse engorgement of sudden onset. Constitutional signs are marked.

There is usually a temperature of 102° to 103°; the pulse is rapid, the tongue furred, the patient feels ill and complains of a headache, lassitude, etc. On examination of the breast the organ is diffusely enlarged, usually very tense, tender throughout, and the overlying skin is flushed and hot. It is doubtful if any improvement in the condition is made without active treatment. With active treatment the condition will often settle completely in a few days, or else pass to the local type of engorgement now to be described.

b. In the local type of engorgement (which may occur spontaneously during lactation, or follow directly during treatment of the diffuse type) constitutional symptoms are similar but less marked. There is a localized tender mass in the breast, the skin over this is red, and the condition is of practical interest in that it may easily be confused with that of localized suppuration.

The treatment of the diffuse type of engorgement is simple and effective. The patient is put to bed when practicable. Local heat may be applied with thermogene wool, antiphlogistine, a linseed poultice, or a hot bottle, and the nipple should not be included in the dressings as it tends to lose both its shape and its firmness. The effect of hot fomentations is too transient to be of value. Hot bathing before attempting to evacuate the breast is helpful, and the breast must be supported between feeds. If the nipple is normal (unusual in these cases), the baby should be fed from the other breast only and the affected breast carefully emptied after feeding. Should there be any pain from direct nipple feeding, then the breast pump must be employed instead. (Attempts at expression are strongly contra-indicated on account of the intense pain produced from pressure on an already tender breast.) Evacuation should be attempted at frequent intervals, at least every three hours, and if possible every two hours. Should this treatment fail, it will usually be because even the breast pump produces intolerable pain on pressure, and cannot be employed satisfactorily.

With regard to the localized type of engorgement, the treatment is from first to last the employment of the breast pump. Local application of heat is unnecessary and appears to aggravate the condition. Rest again is essential, and a breast support is valuable in relieving pain. (It cannot be too strongly emphasized that such support must lift up the breast without compressing it against the chest wall.)

Expression of milk is dangerous in this condition as it is impossible in many cases to tell whether suppuration will occur or not, and it would be unwise to spread the infection in any way.

The breast pump is valuable in evacuating the breast to its fullest extent without in any way interfering with infection if already present. In some rare cases the local condition will discharge via the nipple, even after onset of suppuration.

The use of anti-bacterial measures has often been emphasized in the literature. Before weaning, Benians[1] employed *Sta. aureus* vaccines and found them to be valuable as supplements to evacuation of the breast. Mourgue-Molines[6] employed injections of vaccines together with poultices of ' bouillon vaccin '. Hamm,[15] of Strasbourg, basing his work on that of Besredka,[16] poulticed the skin of the lactating mother with antitoxin as a prophylactic. Whether all these measures are of any value we cannot decide in the Out-patient Department of a large hospital. As a criticism we may say that no attempts at control experiments appear to have been made by these authors.

Unfortunately we have no controls either, and can only state that for ordinary

purposes of hospital work these anti-bacterial measures appear to be unnecessary. After all, engorgement is not necessarily followed by suppuration. Relief of engorgement cannot be obtained by anything but evacuation of the breast. It is possible that where attempts at evacuation fail, the course of infection is less fulminating where the patient's resistance has been raised. However, the whole process of engorgement, if succeeded by suppuration, is such a rapid one that it is doubtful whether the measures of inoculation described will have had time to produce their maximum effect.

We have obtained excellent results in engorgement with the sole use of the simple measures enunciated above.

CLINICAL COURSE OF BREAST ABSCESS

There are various types of breast abscess met with in clinical experience. The superficial or subareolar type of abscess follows a direct infection of subareolar tissue and need not necessarily bear any relation to lactation. The deep abscess is that seen most commonly in direct connection with lactation. The type varies: (a) According to the type of engorgement so commonly a precursor of the condition; (b) According to the virulence of the infection; (c) According to the resistance of the mother to the infection concerned.

As we see it, the course of events is as follows :—

1. Engorgement of the breast is the primary factor in the production of breast abscess.

2. The retained secretion acts as a suitable nidus for organisms which have constant access to the breast, if they are not already present in the ducts.

3. The milky engorgement has already seriously affected the resistance of the functioning glandular tissue, and the peri-alveolar and peri-ductular structures become rapidly involved in the suppurative process.

4. According to the type of engorgement—namely, that generalized throughout the breast, or that localized to one lobe—infection starts in several portions of the breast separately, or in only one place. The progress of infection now depends on the virulence of the infection and the resistance of the patient.

5. Under good conditions the generalized type will localize and multiple well-localized abscesses will result. Under bad conditions, particularly those seen amongst out-patients in London, the whole breast slowly becomes involved in a cellulitis in which localization is poor. Successive areas become involved and break down, and unless active treatment is pursued the whole breast becomes disorganized and ultimately functionless.

6. Where one lobe only remains engorged the infection usually appears to remain localized, and if adequate treatment is adopted, then only that portion of the breast will be affected functionally. If treatment is delayed, then the interlobar septum becomes first invaded, then destroyed, and infection spreads.

7. In any case, should treatment of the condition be inadequate, then either the abscess will burst through the skin and, if still untreated, give rise to a chronic sinus which communicates with disorganized breast tissue, or else the whole breast will become one huge abscess and all functioning elements will be destroyed.

From the above it will follow that one would expect to encounter the following types of abscess :—

1. A diffuse reaction of a cellulitic nature with progressive involvement of tissue, and formation of numerous soft areas containing pus. Constitutional symptoms are probably marked.

2. A breast the seat of one or more localized abscesses with intervening tissue that appears to be fairly normal. The degree of toxæmia varies from case to case. There may be very marked constitutional reaction or practically none at all.

3. A breast that on examination appears to be one huge abscess.

4. A chronic sinus in a breast that has been for some time the seat of suppuration following inadequate treatment.

DETAILS OF TREATMENT

Incision and Drainage.—At one time we believed that there was only one type of treatment suitable for breast abscess—namely, incision and drainage. In consequence we treated our first 42 cases by this means. The procedure was as follows :—

1. When she was in a very toxic condition, we admitted the patient; otherwise we saw her daily in the Casualty Department.

2. If there was definite fluctuation present in the area concerned, we resorted immediately to surgical treatment. On the other hand, if there was a lump present, with redness, tenderness, and indefinite fluctuation, we allowed twenty-four hours with breast support and careful use of the breast pump to see whether by any chance the condition would settle. (We kept notes of five cases of this type that settled, which are not part of the series.)

3. Once incision had been decided upon, the procedure employed was as follows :—

N_2O anæsthesia was employed in all cases. If the abscess was situated above the nipple, an incision radial to the nipple was made at the point of maximum tenderness, and the gloved finger was inserted through this to explore the abscess. All septa were broken down, and the abscess rendered as far as possible unilocular. A counter-incision was then planned and made at the most dependent point—usually at the lower and outer corner of the breast. A long piece of corrugated rubber drain was then inserted well up into the abscess through the lower incision, and kept in position with one salmon-gut stitch, and a dry dressing applied. Where the abscess was situated in the lower quadrant of the breast, only one incision was usually necessary and the abscess was explored from the lower and outer corner of the breast, a drain being then inserted as above.

4. *After-treatment.*—Dry dressings were employed exclusively until the drain was removed, and the wounds dressed twice a day. The co-operation of a district nurse in the first few days is invaluable. The drain is maintained in position until the discharge definitely diminishes and all signs of acute inflammation have disappeared. This may mean maintaining drainage for any length of time up to one week or ten days. It always pays to leave the drain in a long time, and nothing is to be lost by doing so. (This appears to be contrary to the experience of Moon and Gilbert.[18])

Mr. Mitchiner, to whom we have both been House Surgeons, has always condemned hot baths and syringing of the wound as a routine treatment. They

appear to maintain a continuation of the inflammatory process, with pocketing of pus, and in some cases in which they were being employed, a resort to dry dressings instead has resulted in a fall of temperature to normal, and a rapid cessation of local activity.

Two questions arise : (1) When is weaning to be resorted to ? and (2) Should the counter-incision be made through normal breast tissue ?

There appears to be no need for sudden and complete weaning of the baby in every case. It was reserved, in our series, for those cases in which the mother was extremely toxic (notably those cases that were too ill for treatment as out-patients) and those cases that did not appear to be settling after incision as out-patients.

Should the baby be weaned, it is essential to continue evacuating the breast with a breast pump. Ordinarily, we took the baby off the breast concerned and gave it supplementary feeds. As the incisions healed, and all acute inflammation subsided, then it was possible to put the baby back again on the breast.

With regard to the second question, it has long been stated that an incision down to an abscess through normal breast tissue leads to spread of infection to the normal tissue concerned. Shield[14] enunciated the principle that the counter-incision must be made through the
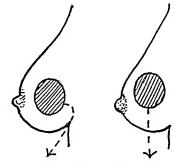
FIG. 444.—Breast abscess. Dependent drainage obtained only by cutting through normal mammary tissue.

inframammary sulcus, with the double advantage that the incision remains concealed and that the normal tissue remains free of superadded infection.

In actual fact the number of cases in which dependent drainage can be established in this way is very small indeed. If practicable, the idea is excellent. As

FIG. 445.—Incision above nipple. No dependent drainage.

shown in *Fig.* 444, dependent drainage can only be established by cutting through normal mammary tissue. In our experience there need be no hesitation in doing this should the necessity arise. We have never seen spread of infection in this manner. If any spread occurs it does so at the upper portion of the breast, owing to lack of dependent drainage.

RESULTS.—We treated in this way 7 abscesses in non-lactating breasts and 35 in lactating breasts.

Non-lactating Breasts.—In the non-lactating cases only 1 gave rise to any difficulty.

Case 1.—Mrs. A. B., of Battersea, aged 22 years, had noticed a lump in the upper portion of the right breast, getting larger and more painful for fifteen days. On examination the abscess was large and situated above the nipple. A somewhat bold incision had been made into a large abscess, with no attempt at dependent counter-drainage (*Fig.* 445).

Considerable hæmorrhage occurred, and the patient had to be admitted for ligature of the bleeding point. Several further incisions were made for pocketing, and the patient was treated for a fortnight with hot baths and the continual applications of hot fomentations. The case was transferred to the Septic Block after fifteen days' treatment. There was continued pyrexia. The breast was soggy and red, with some discharge from various partially healed incisions. All baths were immediately stopped and dry dressings applied instead. The temperature fell to normal in one day and the condition completely settled (*Fig.* 446).

It may well be said that the improvement at this juncture was a coincidence—it possibly was. Nevertheless the case is one for reflection and illustrates well the points to be avoided in the treatment of breast abscess by incision.

The remaining 6 cases settled and were discharged in 8, 7, 10, 3, 6, and 12 days respectively, an average period of treatment of just over a week. These figures bear out our previous statement as to the prognosis in the non-lactating breast.
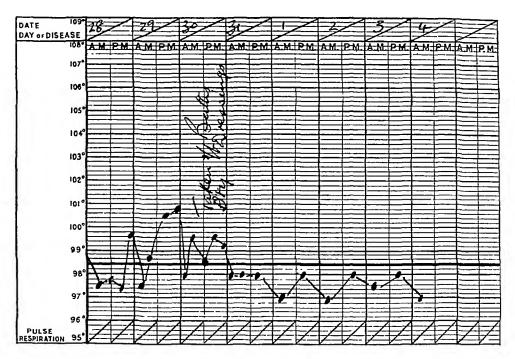
FIG. 446.—*Case* 1. Temperature chart showing effect of discontinuing baths and applying dry dressings instead.

Lactating Breast.—Very different is the prognosis in the lactating breast. Of 35 cases, as many as 11 gave difficulty and required further treatment. There are many factors that might be held responsible for these difficulties. Possibly: (1) The time of onset of infection during the lactation period; (2) The possibility of some particular type of infection associated with a cracked nipple; (3) The abscess occurring in a primipara as opposed to that in a multipara; (4) The abscess that has been neglected until it is allowed to fill the breast or discharge of its own accord; (5) The difficulty of obtaining dependent drainage with abscesses in the upper quadrant. We have examined all these possibilities and come to the conclusion that there are two main factors that complicate successful treatment when this is carried out on the principles mentioned above: (1) The stage which the abscess has reached when first seen by the surgeon concerned. (There is no fixed time factor here, as the condition depends on the subsidiary factors such as the virulence of the infection and the patient's general condition.) (2) The type of infection present. These points are best explained with an analysis of our cases

treated by incision. We have referred above to the various cases met with according to the nature and course of the infection.

1. First, we have the type of single localized abscess occupying one lobe of the breast: 26 of our cases fall into this category, only 7 of which gave any trouble at all. Five of these had to be incised a second time; 1 settled on weaning of the infant; and 1 case developed acute mania of the puerperal type, although there was no difficulty in the treatment of the local condition. (This patient had to be transferred to a mental hospital.)

Of the 5 cases in which re-incision had to be resorted to: in 1 case the drain was removed in the first instance for primary hæmorrhage, and pocketing occurred in consequence; in 1 case at the second operation no pus was found and the case would probably have settled without this second incision; and 1 case flared up six weeks after discharge, apparently on resumption of normal breast feeding. Of the remaining 2 cases that failed to settle, mistaken treatment appeared to be the only factor responsible for failure; 1 case had quite settled and was sent to a convalescent home, where the pernicious practice of ' plugging the abscess ' was resorted to, and in 1 case drainage in the first place was neither adequate nor sufficiently dependent.

2. Secondly, we have the type of multiple localized abscesses. One case of this type was treated by us with incision and only one abscess was drained. At the second operation undertaken for pocketing, an abscess cavity, quite separate from the first, was found, and no further trouble was experienced.

3. Thirdly, there is the most dangerous type of mammary infection—namely, the cellulitis that slowly spreads throughout the breast and breaks down at numerous places. We encountered two of these unfortunate cases :—

Case 2.—Mrs. A. P., aged 31, a primipara, had her confinement on Jan. 25, 1934, in St. Thomas's Hospital. Both nipples cracked soon afterwards and the baby was weaned. Whether the breast was insufficiently emptied, or whether weaning was performed too late, it cannot be decided, but masses appeared in each breast associated with a pyrexia—on the left side on Feb. 8, and on the right on Feb. 12. She was first seen by us on Feb. 12 and was then in an extremely toxic condition, with a hard mass on each side, and was admitted to the Septic Block. Both breasts were repeatedly incised (six times in all). Infected areas were broken down with the finger, and the whole drained at the most dependent point. Following each operation there was a ' flare up ' with a high temperature and rapid pulse, followed by all the signs of settling down. Then the temperature would again begin to swing, and fluctuant areas would appear. The whole condition ultimately subsided completely, after two months of active treatment.

Case 3.—Mrs. A. T. Her first baby was born on April 5, 1934. Both nipples were sore and nipple shields were employed. A lump appeared in the right breast, and was incised on April 20 above the nipple, but dependent drainage was not assured.

The patient was treated elsewhere in hospital for a month and was first seen by us on May 22. At this time the whole breast was involved and there were five separate areas of fluctuation arranged round the nipple. The remainder of the breast was hard and tender. The patient was forthwith admitted to the Septic Block. Incisions were made at each of the fluctuant areas, intermediate tissue was soft and easily broken down with the finger, and the whole cavity well drained. The condition settled immediately, drains were removed on the eighth day, and the patient discharged nearly healed a week later.

It will be stated that this cellulitic condition only arises as a result of mistaken treatment in the first instance. We can but state that such a condition occurs not infrequently and appears to us to be a definite clinical entity in itself. In our view mistaken treatment is most commonly followed by the next types.

4. This type of case is that of the condition that has been left until the whole breast is one large abscess cavity, and is a condition that should surely be avoidable. Three of our cases came into this category of advanced breast abscess. In spite of adequate drainage, two of these had to be incised again. One case was pocketing in the upper quadrant of the breast, and settled with a second incision in the infra-mammary sulcus, and one case pocketed below but also settled with one further incision.

5. The last group of cases is that in which the patient has been allowed to remain untreated until the abscess has burst and a sinus has formed. Three of these cases came under our care. All gave difficulty. Two had to be re-incised, and one settled with general ultra-violet ray treatment only.

The cases that give difficulty are thus firstly that type of infection that produces a cellulitic reaction, and secondly, the type of case that is left for a long time before surgical treatment is attempted. The multiple abscesses should not really be the cause of trouble. Careful search should be made to exclude the presence of a separate small abscess.

The prognosis is good in cases in which, when first seen, the infection is localized to one lobe, and adequate surgical treatment is promptly undertaken.

The results of incision were sufficiently poor to drive us to explore the literature for further and possibly more satisfactory methods of treatment. During this transition period we were able to treat a case by Hamilton Bailey's[3] method, with decided success. Although the method is doubtless excellent for in-patient treatment, it appeared to be rather complex for use in a crowded Out-patient Department, and repeated visits by a district nurse became necessary.

Aspiration.—

a. Treatment with ' Bouillon Vaccin '.—We therefore turned to the method of treatment advocated by Professor Riche and Dr. Mourgue-Molines.[7] This method has the following advantages : (1) General anæsthesia becomes unnecessary; (2) Scarring is not produced; (3) There is no interference with function of the normal breast tissue; (4) The post-operative period is absolutely painless, and close attention to the patient becomes unnecessary, as there are no dressings to be performed; (5) Most important of all, the authors describe a case of the cellulitic type in which treatment completely localized the infection.

The method employed by these workers consists in the aspiration of the abscess and the employment of a bouillon vaccin produced by a firm in Paris, which consists of a filtrate of cultures of staphylococci, etc., according to the type required. The procedure is briefly as follows : The skin over the most tender point in the abscess is infiltrated with novocain. A wide-bore needle is then inserted into the abscess cavity and pus is evacuated. The cavity is washed out with bouillon vaccin, and finally a quantity of the latter—equal to half the amount of pus removed—is left in it.

A profound reaction should ensue. The temperature and pulse should rise, the abscess should become tense and possibly painful over night. The next day, however, the condition should appear more localized, the pain should disappear, together with the more dramatic constitutional symptoms. On the third day, if no further improvement is taking place, the aspiration is repeated. According to the authors, several applications are necessary until the condition has completely

settled. They have obtained quite unusual results, which led us to follow their example, and we were ·fortunate in obtaining permission from the Ministry of Health to import samples of bouillon vaccin from the firm in Paris, to whom Professor Riche had very kindly sent a note on our behalf.

The ' No. 31 ', which was apparently the most suitable of the various bouillons vaccins on the market, formed only a small part of the consignment. Consequently we very rapidly exhausted our small stock, and were forced to employ the other types—designed for such varying diseases as metritis and furunculosis. These acted as excellent controls, and actually produced better results than the ' No. 31 '.

Altogether we had a sufficient supply of bouillon vaccin to treat 21 cases. Two of these cases were in non-lactating patients (in one we used ' No. 31 ' and in the other ' No. 41 '). They both did well, and could be discharged in less than a week each as there was no wound to heal. Of the remaining 19 cases, one must be excluded from the series as we have no record after her first attendance and cannot trace her for follow-up purposes. This leaves us with 18 cases, of which 4 had ultimately to be incised—all lactating patients. One patient failed to report and had to be sent for. On her ultimate return, the condition had progressed, and not understanding very well the scope of aspiration, we decided to resort to incision. One patient reported on the evening of her first attendance with marked constitutional disturbance, a temperature of 102° and a pulse of 120. She was admitted to the Septic Block, the abscess was incised the next day, and settled down quite well without further intervention. We believe that she would have done quite well with further aspiration. Two patients failed to settle with repeated aspirations and even weaning of the infant. They were admitted to the Septic Block and incised and even then failed to settle immediately.

All these four cases were treated with ' No. 31 ', apparently the ideal bouillon vaccin. Our technique was poor, as we had no experience of our subject, and it is possible that, had we treated these cases later in our series, instead of amongst our first 8 or so patients, we would have obtained better results. We did, however, appreciate that there was no specific property to justify the faith reposed in ' No. 31 ' by Riche and Mourgue-Molines. Our control cases, performed with non-specific bouillons vaccins (Nos. 10, 24, 41) had done better. This appeared to confirm the findings of others. Laffont, Fulconis, and Ricard[18] were able to cure 5 cases by aspiration and injection of peptone solution. As the bouillons vaccins are all made up with peptone, it would appear that their effect is possibly one of protein shock.

In one case we decided to do a control with normal saline solution in a patient with bilateral abscesses. We washed out the cavity on one side with saline only, and on the other with bouillon vaccine ' No. 31 '. It required four injections of saline to settle one side, whereas the other side settled with one injection of bouillon vaccin ' No. 31 '. At any rate, we can say that in this case the action of the bouillons vaccins of Riche and Mourgue-Molines was not purely a mechanical one.

We soon ran out of our materials provided through the courtesy of Professor Riche. In order to avoid a prolonged correspondence with the Ministry of Health and heavy customs duties, we resorted to Dakin's solution. In doing so we were on safe ground.

b. Treatment with Dakin's Solution.—Dr. Alejandro Pavlovsky and others have successfully treated breast abscesses with antiseptic solutions. Hobbs[10] has

obtained good results with incision and irrigation with Dakin's solution. Hamilton Bailey[3] employs it in the treatment he describes.

Our method was essentially as described above, without the production of quite the same constitutional reaction in the patient. We were able thus to treat 7 cases ; 2 of these in non-lactating and 5 in lactating patients. Of the former, 1 gave no trouble at all, and the other settled very well on ensuring extra food, and applications of general ultra-violet light.

Of the 5 lactating cases, all did well with one exception. This was a patient in the ward attached to the Venereal Department, who developed a breast abscess on the right side early in the puerperium. The temperature remained exasperatingly high, in spite of several aspirations, and careful washouts with Dakin's solution. There were practically no signs in the other breast except slight tenderness and possibly a fullness in the upper and outer quadrant. Finally we explored the other breast with a needle, evacuated somewhat to our surprise 30 or 40 c.c. of pus, and washed out the cavity. The temperature still did not fall, and under N_2O anæsthesia we incised an enormous abscess and drained it from the most dependent point. The temperature then settled at once, and although the breast discharged over a long period, the wound was healed within one month of commencement of the trouble.

It appears impossible at first for the person who is wont to incise breast abscesses to understand that adequate drainage can possibly be maintained by repeated aspirations. We started this treatment under strong criticism, and with serious doubts in our minds as to the efficiency of methods described by the various authors we read.

J. W. S. H. Lindahl, until recently the House Surgeon to the Septic Block, has successfully treated quite a number of cases by aspiration and washing out with Dakin's in the same way.

Technique.—The exact technique employed in treating a case by aspiration is not of particular importance. Anybody who tries this method will sooner or later employ a technique of his own according to the instruments and facilities at his disposal. That which we describe here is one which we have developed ourselves, and which we trust may prove of value as a starting point to any persons interested in this method. When it was decided to aspirate the abscess, the baby was immediately taken off the breast concerned and given complementary feeds when necessary. Care was then taken that all milk forming in the affected breast should be removed at regular intervals with the aid of the breast pump. The syringe employed is of a capacity of about 25 c.c., to which may be attached a needle of wide bore. We have employed needles of a diameter of 2·5 mm., and like to have at least two, and preferably three, of these ready, sterilized for use with every case. The best type of syringe is that in which the needle is attached by a ' Luer ' fitting, the ' record ' attachment being too narrow to allow successful passage of sloughs into the barrel.

The breast is cleansed with ether and the surrounding area packed off with sterile towels. The point at which aspiration is being performed must then be chosen. This point is that at which fluctuation is present. If seen early the abscess should be aspirated at the point of maximum tenderness. The area chosen is then infiltrated with 2 per cent novocain down to the abscess cavity, which is easily recognized owing to the facility with which the anæsthetic enters. The plunger of

the 'record' syringe is then withdrawn and the position of the needle is often confirmed by the withdrawal of pus.

A wide-bore aspiration needle is then inserted through the anæsthetized area into the abscess cavity and pus withdrawn. The needle is left in position, the pus in the syringe is emptied out, and an equal quantity of Dakin's solution diluted to half strength with sterile water is inserted again via the needle *in situ.*

Should the needle become blocked during aspiration, the syringe should be emptied again gently towards the abscess cavity, or else more Dakin's solution should be injected. It should never be necessary to remove the needle until the whole procedure is accomplished. In this way the cavity should be washed out until the fluid in the syringe is nearly clear, and at any rate until no more debris and sloughs are recognizable in the fluid removed. The abscess cavity should be left empty, and by withdrawal of sloughs it is hoped that the walls may be allowed to fall together.

After the aspiration the point of entry of the needle should be covered with the minimum dressing and the breast supported with a proper sling bandage. There is no need for any further local treatment now until the patient reports for further inspection in about twenty-four hours' time.

One aspiration is often sufficient in treating the small superficial abscesses, but for the commoner case of deeper abscess, repeated aspirations are usually necessary. Here are the indications for further aspiration :—

1. *Continued Pyrexia.*—When present alone without local signs, aspiration can be deferred for a further twenty-four hours, particularly when leakage is occurring through the puncture in the breast.

2. *Pain.*—Pain in the breast concerned is immediately relieved by aspiration of the abscess cavity and is evidently merely the result of tension. With return of pain aspiration is indicated.

3. *Local Tenderness.*—If it persists, or if it returns, this is a strong indication for further interference.

We would emphasize that in the absence of these indications aspiration need not be repeated. We have found in our own experience that there is a strong temptation to repeat aspirations quite unnecessarily, and careful consideration should always be given to the case before further aspiration is attempted.

Failure to settle after two or three aspirations *is not* uncommon. Several considerations must now be borne in mind, and we have proceeded on the following lines :—

1. Weaning of the baby. Several of our cases have settled on complete weaning without further aspiration. In these cases, of course, it is essential that both breasts should be kept carefully emptied by means of the breast pump.

2. The general condition of the patient must be considered. Remarkable improvement will sometimes be seen when extra nourishment is provided in the form of milk, eggs, etc. In all cases we have prescribed alcohol where possible, preferably in the form of the malted liquors. General applications of ultra-violet light have appeared to be valuable in the only two of our cases in which they have been tried.

3. Cases are frequently met with in which several loculi drain into a main abscess cavity, and which continue to maintain signs of activity in the breast when the main abscess cavity appears to be quite settled.

When first seen these cases may present two or more areas of tenderness, widely separated from each other. It is as well, then, to aspirate each cavity separately with a needle inserted at these points and then with the needles *in situ* to wash the Dakin's solution to and fro between the separate loculi.

Should the area of tenderness, or presence of fluctuation, suggest that some loculus is maintaining the toxæmia, then it is essential that these areas be explored and carefully washed out. In one of our cases we found as many as four different loculi forming separate abscesses in close contact with each other. Fortunately the condition was recognized early and the case settled well without the necessity for incision.

Finally, if in spite of these considerations, the case fails to settle after repeated aspirations, resort must be had to incision, which we carried out in our series on the lines indicated in the first section of this article. As we increased our experience of aspiration, we found that the number of cases which failed to settle with this treatment very greatly decreased in number. Nearly all our failures occurred amongst our early cases. It should also be stated that all our cases of aspiration were treated as out-patients.

CONCLUSIONS

It has been stated elsewhere[19] that variations in local treatment by different surgeons is of no significance. We cannot agree with this statement, and have found that increase of experience in the treatment of intramammary abscess is accompanied by improved results. Consequently we have entered into considerable technical detail in this series of cases, some of which we have treated with incision and some with aspiration.

We have described a method of aspirating breast abscesses and washing them out with Dakin's solution. Abroad, certain ' bouillons vaccins ' have been employed with conspicuous success. To import these it is necessary to obtain special permission of the Ministry of Health and to meet customs obligations. Dakin's solution has been found to give good results, and is of easy access to any practitioner in this country.

It now becomes necessary to review the whole series of cases and to attempt some impartial judgement between the merits of incision and those of aspiration.

1. The aspiration of an abscess is a procedure that can be performed single-handed without skilled assistance. The anæsthetic employed is a local one, there is no wound to be dressed afterwards and the co-operation of a district nurse becomes unnecessary. Scarring is reduced to a minimum, and consequently the ultimate cosmetic and functional result is of the best. Aspiration is therefore to be preferred in those cases of suppuration occurring in the non-lactating breast and in those cases in which, during lactation, the abscess is relatively localized and confined to one lobe.

2. With the very large abscess and neglected breast, incision immediately relieves an already prolonged toxæmia and drains a large cavity more satisfactorily than can aspiration.

3. With the diffuse, cellulitic type of infection the prognosis is poor, however the condition be treated. Incision is probably to be preferred, in that by this means the local condition can be thoroughly explored with the finger and infected areas broken down into one large abscess cavity.

4. Should any doubt be entertained as to the treatment necessary with any particular case, we advise the use of aspiration. At the worst incision can always be resorted to with failure to settle after several aspirations, and only time is lost.

In conclusion we should like to record our indebtedness to many who have helped us directly and indirectly with the preparation of this article : Mr. P. H. Mitchiner, to whom we were both House Surgeons in the Septic Block of St. Thomas's Hospital, for the permission to use his cases and for his excellent advice and friendly criticism; Professor Riche, who very graciously gave us an introduction to the Maison Gremy of Paris, so that we could obtain a supply of bouillon vaccin; Dr. Doyne Bell for his help with difficulties encountered in the writing of this article; Drs. J. P. Hedley, R. Jewesbury, J. Wyatt, P. A. Clements, and J. Wrigley, for permission to quote cases of theirs which we have treated in this series; and Mr. J. W. S. H. Lindahl for his help in the correction of proofs. Finally, we would particularly thank Miss Annie Beal and her staff in the Casualty Department for their untiring support, and also Miss Routh, sister-in-charge of the Septic Block, whose knowledge of the nursing of septic cases must be unrivalled in this country.

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VISITS TO SURGICAL CLINICS AT HOME AND ABROAD

MR. H. B. DEVINE AT ST. VINCENT'S HOSPITAL, MELBOURNE

DURING the recent visit of the British Medical Association to Melbourne on the occasion of their Annual Meeting we had the opportunity of seeing the work at the hospitals, both in the city and in the outlying seaside annexes. One is conscious of the fact that the rush of meetings and festivities does not afford the opportunity for quiet observation that one would wish for, nor does it allow for an adequate appreciation or description of the hospitals and surgical clinics of a great city. But, on the other hand, one was so much impressed by the excellence of the work, that one cannot do less than give a brief description of the clinics of one of the leading surgeons who is so largely responsible for the high surgical standards in the capital city of Victoria.

Melbourne, a spacious city of over a million inhabitants, has four main hospitals, the Melbourne, the Alfred, the St. Vincent's, and the Children's. At present there is no close association between these hospitals or between them and the University, each hospital taking a certain number of students, who are examined for their degree at the University. Nor is there a Professor of Surgery at Melbourne, the senior surgeons of the three general hospitals acting as lecturers and examiners for the University.

The St. Vincent's Hospital of 250 beds has recently been rebuilt and represents the last word in up-to-date hospital architecture. The institution is a 'voluntary' hospital, but the patients pay towards the cost of their maintenance and there is an ample provision of wards for private patients.

On Tuesday, Sept. 10, Mr. Devine operated before a large number of spectators, including many members of the British Medical Association.

1. **Gall-stones : Cholecystectomy** (2.30 to 3.15 p.m.).—Woman, aged 61, high blood-pressure, enlarged liver. Anæsthesia by ether. Mid-line incision 6 in. long. Edges of incision protected by sponge cloths and drawn aside by retractors held on a square metal frame (*Fig.* 447). (The use of this frame retractor plays a prominent part in all Devine's abdominal work. Various types and shapes of retractor can be adjusted to any of the four sides of the square. It gives a splendid view of the abdominal cavity and makes it unnecessary to touch or handle any of the viscera.) The gall-bladder full of stones was well exposed, whilst the liver and intestines were packed away and held by covered retractors. The cystic duct and artery were exposed and ligatured and the gall-bladder was removed with a few touches of the scissors. The abdominal wound was closed in layers with catgut.

2. Colostomy for Inoperable Growth of Colon (3.30 to 4 p.m.).—Man of 50. Typical symptoms. Growth demonstrated by X rays to be in the splenic flexure. Vertical incision over the right rectus. There was a good deal of free
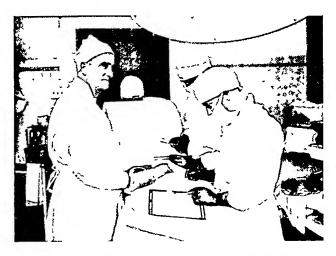
FIG. 447.—Mr. Devine operating. The photograph also shows the square metal frame retractor used for abdominal surgery.

fluid and a sucker was inserted into the lower angle of the wound. The hand, well smeared with vaseline, was inserted for exploration. The growth was felt to be inoperable and therefore a colostomy was decided upon. The hepatic flexure

FIG. 448.—Mr. Devine conducting a students' clinic.

was mobilized and brought to the surface. A large tube was passed through the mesocolon to hold the gut on the surface. The two limbs of the loop were sewn together proximal to this. Two Kocher's forceps were applied across the gut,

which was divided by a diathermy knife. A skin-flap was then fashioned from the outer part of the abdominal incision and turned up so as to lie between the two divided ends of the colon. This skin was sewn in place and was made to surround each stoma tightly. Both clamps were left on ; that on the proximal end was to be removed in twenty-four hours, whilst that on the distal was left till it came off.

3. **Carcinoma of Male Breast : Radical Removal** (4.15 to 5 p.m.).—Man, aged 63. Nodule medial to nipple on left breast. General anæsthesia. Skin incisions first marked out by light cuts. Wide area of skin removed. Diathermy not used because of the danger to vein. Dissection done entirely by the scissors. Axilla cleared first. The breast and axillary contents having been

FIG. 449.—The Royal Australasian College of Surgeons, Melbourne.

removed, the vessels were ligatured with silk. The large raw area left was closed first by turning down a flap of skin from the chest and then by a number of Thiersch grafts taken from the right thigh. These were covered by tin-foil over which pieces of rubber sponge were placed to maintain pressure.

The wards of St. Vincent's Hospital are large and well lit. The nursing is by the sisters of St. Vincent de Paul. Ward rounds, well attended by students, give great scope for Devine's teaching faculty (*Fig.* 448). He is on the most friendly terms with his dressers and house surgeons, and obviously has impressed them all with a great sense of loyalty and devotion.

It would not be fair to close this very brief and inadequate account of Devine's work without referring to two other directions in which his energies have made

themselves felt in the surgical world of Australia. The first of these is the Royal Australasian College of Surgeons (*Fig.* 449), opened at the beginning of this year by Sir Holbert Waring. Both Hamilton Russell and Sir Richard Stawell were active in initiating the movement for the foundation of the College. But no one has done more in an unobtrusive way than Devine for securing the ground and the funds, and, above all, reconciling conflicting views and inspiring the ideal which underlies this College. It is a dignified red brick structure splendidly situated in a wide open space quite near to the Parliament House. Dr. Wade, of Sidney, is the President of the College, and Mr. Allen Newton shares with Mr. Devine the greater part of the work of planning and organization.

The second great piece of constructive surgical work which stands to Devine's credit is the foundation and editing of the *Australasian Journal of Surgery.* It is a great and ambitious undertaking for a country of the population of Australia and New Zealand, and in its successful conduct we wish H. B. Devine every success.

EXPERIMENTAL SURGERY

THE INFLUENCE OF ŒSTROGENIC COMPOUNDS IN CAUSING HERNIA AND DESCENT OF THE TESTIS IN MICE

By HAROLD BURROWS

RESEARCH INSTITUTE, THE CANCER HOSPITAL (FREE), LONDON

THE causation of scrotal hernia in mice by the administration of œstrone (œstrin) was described by the author in a previous number of this JOURNAL.[1] Since that article was written, further observations have been made in this branch of pathology which are perhaps worth recording.

1. **Scrotal Hernia not Found in Mice apart from the Administration of Œstrogens.**—A matter of importance was to learn how often, if at all, scrotal hernia might develop in mice which had not been submitted to any œstrogenic compound. For this purpose 4013 male mice of all ages were examined. Some of them were untreated mice, others had been grafted with tumours or subjected to various tests in connection with the production of cancer; none of them had received applications of any œstrogen. No instance of scrotal hernia was discovered in the whole of this series. The appearance of scrotal hernias in mice after the administration of an œstrogenic compound may therefore be safely attributed, it seems, to the action of that compound.

2. **Substances which Cause Hernia in Mice.**—In the course of our experiments eight different œstrogenic compounds, chemically pure, have been found to induce hernia. Their relative capacities for causing hernia vary, and seem to correspond to some extent, though not entirely, with their œstrogenic potency. More precise statements cannot be based on the experiments now in consideration; the great majority were designed for another purpose than the study of hernia formation and consequently did not include a regard for all the details which would be necessary for an exact study of the comparative potencies of different œstrogens to cause hernia. The compounds found to be capable of inducing scrotal hernia in mice are œstrone (œstrin), œstrone methyl ether (ketomethoxyœstrin), œstradiol (dihydroxyœstrin), œstriol (trihydroxyœstrin), equilin, equilenin, 9 : 10-dihydroxy-9 : 10-di-*n*-propyl-9 : 10-dihydro-1 : 2 : 5 : 6-dibenzanthracene (Cook, Dodds, Hewett, and Lawson[2]), and a similar compound with butyl substituted for propyl (Cook[3]) (*Fig.* 450).

Among compounds which, having some similarity of structure to the œstrogens, are not œstrogenic and do not cause hernia, are androsterone (male sex hormone), progesterone (hormone of the corpus luteum), pregnandiol, and deoxycholic acid. The formulæ of these are given for comparison with those above (*Fig.* 451).

3. Additional Observations on the Production of Hernia by Œstrone.—
Since the previous paper on hernia in mice was written, further observations have
been made with œstrone. A hundred more male mice have been treated with
bi-weekly applications of œstrone (0·01 per cent in benzene) to the skin of the
back: 22 early deaths occurred in this group, and among the 78 survivors hernia
occurred in 47.

CESTRONE   ŒSTRONE METHYL ETHER   ŒSTROL   EQUILIN
(KETOHYDROXY-   (KETOMETHOXYŒSTRIN)   (TRIHYDROXYŒSTRIN)
ŒSTRIN)

EQUILENIN   ŒSTRADIOL   9 : 10-DIHYDROXY-9 : 10-DI-*n*-
   (DIHYDROXYŒSTRIN)   PROPYL-9 : 10-DIHYDRO-1 : 2 : 5 : 6-
     DIBENZANTHRACENE

FIG. 450.—Formulæ of œstrogenic compounds which cause hernias in mice.

a. Effect of Non-descent of the Testis.—An early question to arise was why
hernia should appear in some mice and not in others treated in exactly the same
way with œstrone. It was noticed that hernia occurred most readily in those mice
whose testes were fully developed and lying well down in the scrotum when the
applications of œstrone were begun. Most of our experiments were carried out
on young mice freshly arrived from the dealer, and said to be between 5 and

PREGNANDIOL   PROGESTERONE   ANDROSTERONE   DEOXYCHOLIC ACID
   (PROGESTIN)

FIG. 451.—Formulæ of compounds allied to those of *Fig.* 450, but which do not
cause hernias or artificial œstrus in mice.

6 weeks old. Among 1410 of these mice examined consecutively, the testes were
undescended in 427. When such immature mice with undescended testes are
submitted to regular bi-weekly applications of œstrone, some of the testes come
down into the scrotum, but many remain undescended so long as the treatment
with œstrone is maintained; and as long as the testes remain in the abdomen no
hernia occurs. Two facts seem to have emerged: (i) The presence of a more or
less mature testis is necessary for the formation of scrotal hernia under the influence

of œstrone; (ii) Œstrone may prevent descent of the testis, which in this event fails to become mature, as shown by its small dimensions and by the absence of spermatogenesis.

Hernia does not invariably follow the application of œstrone even when the testes descend into the scrotum (*see Table II*). The explanation of this must await an opportunity to examine the testes at the time when hernias first appear in a group of mice submitted to the necessary œstrogens.

b. Effects of Artificial Cryptorchidism.—Thirty-eight mice whose testes were fully descended were rendered cryptorchid by dividing the gubernaculum on each side and displacing the testes into the abdomen. In 18 of the mice the operation was performed by means of a laparotomy wound so as to avoid injury to the scrotum, and in 20 the exposure was made through the scrotum. Of the 38 mice treated in this way, 28 were given applications of œstrone, and 10 were kept as controls. Hernias subsequently occurred in 15 of the mice treated with œstrone, and no hernia occurred among the controls (*Table I*).

Table I.—EFFECTS OF ARTIFICIAL CRYPTORCHIDISM COMBINED WITH APPLICATIONS OF ŒSTRONE

NUMBER OF MICE	SITE OF OPERATION	SUBSEQUENT TREATMENT	MICE WITH HERNIA
18	Abdomen	Œstrone	9
10	Scrotum	Œstrone	6
10	Scrotum	None	0

Sixty-eight days after the operation on these mice there were 34 survivors, of which 25 had been treated meanwhile with œstrone, and 9 had not been given œstrone. Among those treated with œstrone descent of the right testis had occurred in 19 and descent of the left in 18. Among the 9 which had received no œstrone the right testis had descended in 8 and the left in 6. In most and perhaps in all the instances in which retention occurred it was attributable to fixation of the testis in the abdomen by post-operative adhesions.

In some of the mice in this experiment a bilateral hernia was found, although one of the testes had been retained in the abdomen by post-operative adhesions. In one instance the left testis had failed to descend because of adhesions, and the right testis had descended into the left scrotum. In another mouse both testes had come down into the left scrotal pouch. In both of these mice bilateral hernias were present. These observations show that a gubernaculum is unnecessary for the descent of the testis, though it is indispensable as a guide to a correct disposal of the testis in the scrotum. Further, although a well-developed testis is necessary for the production of a scrotal hernia by œstrone, that testis need not itself be in the scrotum at the time of formation of the hernia.

c. Effect of Unilateral Castration.—To elucidate the matter, the right testis was excised from 10 mice, and applications of œstrone were thereafter made to them and to 10 intact controls. Bilateral hernias appeared in 4 of the survivors of the mice with a single testis and in 6 among the 10 which had not been castrated (*Table II*).

Table II.—EFFECTS OF APPLYING ŒSTRONE TO MICE HAVING ONE TESTIS ONLY

NUMBER OF MICE	PRELIMINARY TREATMENT	SURVIVING AFTER 65 DAYS	NUMBER WITH RETAINED TESTIS	MICE WITH BILATERAL HERNIAS
10	Unilateral castration	5	1	4
10	None	10	1	6

In each series no hernia occurred in the mouse with retained testis.

d. Effect of Bilateral Castration.—The testes were removed from 30 mice, which were thereafter treated with applications of œstrone till their death. In none of these mice did any hernia appear.

e. Effect of Vitamin Deficiency.—The healthy development of seminal epithelium is dependent upon adequate supplies of vitamins in the diet. Vitamin E is of particular importance, a deficiency leading rapidly to degeneration of the seminal epithelium. Ten mice were placed on a diet deficient in vitamin E, and another 10 were given a diet of white bread only, and both these series were thereafter treated with œstrone in the usual way. A heavy mortality ensued. At the end of six weeks only 3 of the mice on a vitamin E deficient diet remained alive, and none showed a scrotal hernia, though the period of treatment was sufficiently long for such a development. Of the mice kept on a diet of white bread, 5 survived for three months or more, and no scrotal hernia developed (*Table III*). Among 10 control mice treated with œstrone and given a normal diet, hernias developed in 7.

Table III.—EFFECT OF VITAMIN-DEFICIENT DIETS IN PREVENTING HERNIA IN MICE TREATED WITH ŒSTRONE

NUMBER OF MICE	DIET	SURVIVING FOR 6 WEEKS OR MORE	MICE WITH HERNIA
10	Vitamin E deficient	3	0
10	White bread only	5	0
10	Normal	9	7

In a later experiment 30 mice were treated with bi-weekly cutaneous applications of œstrone benzoate (0·01 per cent in benzene). Thirteen weeks after the commencement the results were as shown in *Table IV*.

Table IV.—PRODUCTION OF HERNIA BY ŒSTRONE BENZOATE

NUMBER OF MICE	DIET	SURVIVING AT END OF 13 WEEKS	RETAINED TESTES	MICE WITH HERNIA
20	Normal	16	0	5
10	Vitamin E deficient	4	4	0

f. The Effects of Long-continued Applications of Œstrone.—In some cases the hernias have progressively increased so as to reach very large dimensions, and there have been several instances in which almost all the abdominal contents except parts of the liver and stomach have become transferred to the scrotum. In examples of this kind the entire spleen is sometimes found in the right scrotal pouch and sometimes in the left. Even large hernias have diminished in size on cessation of the dosage with œstrone, though they have not disappeared. Small hernias which have not long existed will become cured spontaneously if no more œstrone is given.

When considering the effects of repeated dosage with œstrone it has to be borne in mind that mice show considerable differences in the rapidity and degree with which they respond, and also that with long-continued dosage there appears to be a tendency to develop some resistance to the hormone.

DISCUSSION

In the foregoing investigation œstrone was supplied in quantities much in excess of those which occur naturally. The gross effects of the treatment on the mamma and generative organs are proofs of this. The experiments show that œstrone will bring about a scrotal hernia in the mouse only if a testis is present and is in a mature or nearly mature condition. Perhaps this may explain to some extent the descent of the testes in animals during rut, the experimentally induced scrotal hernia representing an artificial exaggeration of the natural process. Most, if not all, the changes induced by œstrone are reversible, and hernia is not an exception unless of long standing or large.

It is not easy to explain why in some instances the continued application of œstrone should lead to a progressive increase in the size of a hernia, seeing that : (1) the occurrence of hernia is associated with a well developed seminal epithelium ; and (2) œstrone has a restraining effect on the seminal epithelium. Some mechanism, at present obscure, must come into play to account for these phenomena. The inhibitory effect of œstrone upon the seminal epithelium is thought to be exercised indirectly through the anterior lobe of the pituitary gland. The active phases of the seminal epithelium appear to be brought about by a hormone derived from the pituitary gland, and it is believed that œstrone inhibits the output of this hormone (Moore[4, 5]). On the other hand, prolan is thought to stimulate the pituitary to elaborate this hormone. Such reasoning provides a basis for the use of prolan in the treatment of undescended testis ; though, in a tentative experiment performed by the author with Mr. F. L. Warren, three successive daily doses of 77 mouse units of a commercial preparation of prolan failed to cause descent of the testes in any one of four mice whose testes had not descended naturally. The necessity for the presence of a well-developed seminal epithelium in order that œstrone may induce a scrotal hernia may be borne in mind when the causes of non-descent of the testis in boys are under consideration. The seminal epithelium is readily damaged, not only by excess of œstrone, but by dietary deficiencies and other adverse circumstances (Mason[6]).

It has been suggested that, as œstrone may cause distension of the bladder and hydronephrosis, the hernias may be the consequence of increased mechanical pressure during efforts at micturition. Such a suggestion can be met by the

following facts : (1) Attempts to produce scrotal hernia by digital pressure on the abdomen, whether in living or freshly killed mice, have always failed. (2) The hernias induced by œstrone may appear early, having been seen exceptionally after three applications only; vesical distension is a much later consequence. (3) Castrated mice treated with œstrone, and mice whose testes are retained in the abdomen through the continued administration of œstrone, not infrequently succumb to hydronephrosis but do not have hernia. (4) Hernias were not present in two mice which died of urinary obstruction caused by scars resulting from fights.

Additional experiments are needed to elucidate the precise condition required in the testis in order that œstrone may cause hernia. Examination of the testes of a series of mice at the time that hernias are appearing is one of these. Another desirable experiment would be the unilateral castration of immature mice, to be followed by the administration of œstrone after maturity and descent of the remaining testicle have come about. The object of this would be to ascertain whether a preliminary descent of the testis is essential for the subsequent induction of scrotal hernia by œstrone. These additional experiments must await some future opportunity.

A fact that touches on the problem is that some œstrogens (equilin, œstradiol) cause a great increase of the interstitial tissue of the testis with degeneration of the tubular epithelium. These changes occur whether the testes are retained or not, and appear inimical to the development of hernia. Although either of these compounds may cause hernia in mice whose testes are already in the scrotum, they seldom caused hernia in mice whose testes had not come down at the commencement of the application. From this experience it appears that the interstitial tissue of the testis does not co-operate with the œstrogen in the induction of hernia.

One more observation may be added to the foregoing; it has reference to strangulated hernia. The aperture between the scrotal sac and the abdominal cavity in mice is not a narrow one, and strangulated hernia has not been seen. Death has occurred in two instances from intestinal obstruction, caused in one case by torsion of the cæcum within the hernial sac, and in the other by torsion of a loop of small intestine within the sac. No adhesions were present in either instance.

SUMMARY

1. Scrotal hernia rarely if ever occurs spontaneously in mice.
2. Every potent œstrogenic compound tested has induced hernias.
3. Hernia has not been induced by any non-œstrogenic compound.
4. Œstrone will induce hernia only if the testis is nearly or quite mature.
5. Œstrone tends to inhibit descent of the testis and to prevent it from maturing.
6. In immature mice œstrone may prevent descent of the testis. In these cases hernia will not appear.
7. Only one testicle is necessary for the development of bilateral hernias under the influence of œstrone.
8. Bilateral castration prevents the production of scrotal hernias by œstrone.
9. Vitamin deficiency, which damages the seminal epithelium, prevents the production of hernia by œstrone.

10. Scrotal hernias may enlarge progressively as long as the dosage with œstrone is continued.

11. Unless large or long existent the hernias disappear after cessation of the supply of œstrone.

12. The gubernaculum is not essential for the descent of the testis. It is a guide, and in its absence the testis may descend into the wrong scrotal pouch.

13. The causation of hernia by œstrone is regarded as an exaggeration of the natural process of descent of the testis.

I have great pleasure in mentioning my indebtedness to my colleagues for help and advice in carrying out this study. The chemical basis of the work has depended entirely on Professor J. W. Cook. The maintenance of mice on a diet deficient in vitamin E was kindly supervised by Dr. E. Boyland. To Dr. Girard particular thanks are due ; without his generous gifts of œstrone, œstradiol, equilin, and equilenin, much of the work could not have been done. For a supply of œstriol (theelol) I am indebted to Messrs. Parke, Davis & Company, and for additional supplies of œstradiol to the Organon Laboratories.

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AN EXPERIMENTAL METHOD OF PROVIDING A COLLATERAL CIRCULATION TO THE HEART

By LAURENCE O'SHAUGHNESSY

RESEARCH LABORATORIES, ROYAL COLLEGE OF SURGEONS OF ENGLAND AND THE
BUCKSTON BROWNE SURGICAL RESEARCH FARM

OF recent years the clinical importance of the collateral blood-supply to the heart has been emphasized by the work of Hudson, Moritz, and Wearn. It appears that obstruction of the main stem of a coronary artery is compensated for by collateral channels from the remainder of the coronary circulation, as well as by collaterals from the general systemic circulation, which reach the heart from the mediastinum. There are connections between the coronary system and the pericardiaco-phrenic artery and the anterior mediastinal, pericardial, bronchial, and œsophageal branches of the aorta. It is clear that in many cases this collateral circulation is inadequate, and the infarcted area in the heart wall progresses either to an acute rupture within the space of a few days or to the formation of a cardiac aneurysm, rupture of which may be delayed for an indefinite though usually limited period. In other cases ischæmia of the myocardium is followed by permanent cardiac incapacity.

The problem of increasing the collateral blood-supply may be approached in several ways. The efficiency of the collateral supply from the coronary system depends on the measures adopted at the moment of occlusion. In the experimental work of Leriche it appears that maintenance of the systemic blood-pressure is of decisive importance; the issues raised by this concept are the subject of investigations still in progress.

Various experimental methods have been adopted to increase the efficiency of the extra-cardial anastomoses. The simplest method is to promote the formation of pericardial adhesions by the application of some irritant to the endothelial lining of the sac. Beck has reported an experiment in which he removed the epicardium and so promoted the formation of adhesions between the fibrous pericardium and the surface of the heart, and his animal subsequently tolerated almost complete obliteration of the coronary arterial tree. The method described in this paper is the application of a large omental graft with its vascular pedicle in the abdomen.

The great omentum was selected as the appropriate agent for several reasons. Personal experience with the Morison operation for ascites had impressed me with the capacity of the pedicled omental graft to form new vascular attachments. In a previous paper (1933) the use of the pedicled omental graft in experimental resection of the œsophagus has been described. At a later date Ohsawa has, quite independently, recorded his successful experience with the pedicled omental graft in resection of the thoracic œsophagus in man. The method of the experiments, carried out in the cat and the dog, is as follows. Anæsthesia is induced with chloroform and maintained with oxygen and ether under positive pressure. The

left chest is entered by a long intercostal incision and the surface of the heart exposed by incision of the fibrous pericardium. An incision is made in the left leaf of the diaphragm in the direction of its fibres, and the abdominal cavity explored until the stomach and omentum are exposed. A large segment of the omentum is separated from the rest of the organ, care being taken to avoid injury to the contained vascular trunks, and the graft so obtained is attached to the surface of the heart by one or two fine sutures (*Fig.* 452). The wound in the diaphragm is

FIG 452 —The graft in place

closed by a single suture in such a way as to avoid pressure on the vascular pedicle of the graft. The fibrous pericardium is not sutured, and the chest wound is closed in layers.

The technique of the injection studies is based on that described by Bromer, Zschiersche, and Wearn. The injection, at a pressure of 150 mm. Hg, was made into the abdominal aorta immediately after death with indian ink diluted with an equal quantity of distilled water. The heart was removed from the chest by severing the aorta and its other vascular connections, until its only attachment to the animal was by the omental graft.

The operation was done on fourteen cats and two dogs, and although some of the animals had been previously subjected to ligature of the coronary artery, in no case was any immediate post-operative distress observed. One animal subjected to ligature of the descending branch of the left coronary artery died of acute œdema of the lung ten days after operation, and another died fourteen days after operation from obstruction due to prolapse of the small intestine into the left chest through the wound in the diaphragm. In a large series of experiments with the pedicled omental graft this was the only accident of the kind observed. In all the other specimens studied at post-mortem the omentum was firmly adherent to the margins of the opening in the diaphragm.

There follow the protocols of several experiments of special importance.

FIG. 453.—*Dog* 1. Greyhound heart with graft in position.

Dog. 1 (greyhound, aged ?).—

8.1.35.—Operation : ligature of descending branch of left coronary artery.

15 4.35.—Exercise tolerance tested on track. After completing the course the dog appeared rather more distressed than a normal animal as judged by colour of tongue and respiration rate.

16.4.35.—Operation : pedicled omental graft applied to area of old infarction in heart wall.

12.9.35.—Exercise tolerance again tested on track. Performance normal and no distress on completion of run.

30.9.35.—Animal killed and graft found in position. Arteries injected with cinnabar paste. (*Fig.* 453.)

Dog 2 (greyhound, young).—

21.3.35.—Operation : ligature of descending branch of left coronary artery.

28.5.35.—Operation : pedicled omental graft.

12.9.35.—Exercise tolerance tested on track.   Running capacity normal, run finished in very good order.
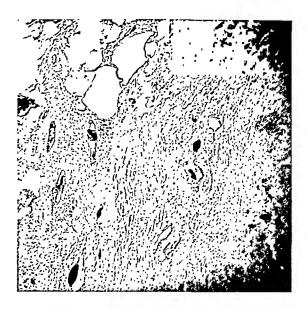
FIG. 454.—*Cat* 3.   Injection of vessels in omentum and superficial layer of myocardium.
(× 50.)
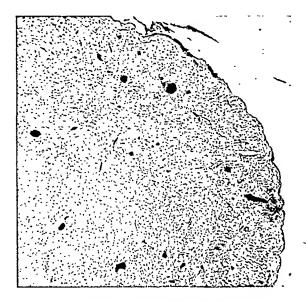
FIG. 455.—*Cat* 4.   Injection of vessels beneath endocardium. (× 50.)

Cat 3.—

27.6.35.—Operation: pedicled omental graft.

24.9.35.—Killed and specimen injected (*Fig.* 454).

Cat 4.—

29.6.35.—Operation: ligature of descending branch of left coronary artery and pedicled omental graft.

25.9.35.—Killed and specimen injected (*Fig.* 455).

FIG. 456.—*Cat 5. Injection mass lying in lymphatic spaces in myocardium. (× 50.)*

Cat 5.—

16.2.34.—Operation: ligature of descending branch of left coronary artery.

16.7.35.—Operation: pedicled omental graft.

25.9.35.—Killed and specimen injected (*Fig.* 456).

A method has been described by which a collateral circulation to the heart may be established in the experimental animal. On injecting Indian ink suspension into the heart through the graft, particles of ink could be seen emerging from the cut aorta. In some of the sections vessels filled with ink may be seen lying immediately beneath the endocardium, and particles of the suspension are seen lying free in the chambers of the heart.

We have no data as to the length of time required for the new vascular connection to form, but in one animal killed three weeks after application of

the graft a very complete injection of the coronary arterial tree could be carried out.

At the beginning of this work some two years ago, it was intended to establish the functional importance of the pedicled omental graft in experimental coronary occlusion. For various reasons this intention has been abandoned. Observations on experimental coronary occlusion showed that many animals tolerated the procedure well, and the factors governing the occasional incidence of acute œdema of the lungs, pulmonary embolism, and acute heart failure remained unknown, so that a control group of animals could not be observed. At the same time the tests performed by the two dogs at least demonstrate that recovery from the operation is compatible with severe physical exertion.

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SHORT NOTES OF RARE OR OBSCURE CASES

SARCOMA OF ACETABULUM MISTAKEN FOR TUBERCULOUS HIP

By C. H. FAGGE
CONSULTING SURGEON, GUY'S HOSPITAL

LEONARD M., age 34, was first seen by Dr. A. H. Warde, of Purley, in April, 1934, when he complained of pain in the groin and the inside of the right thigh; the pain extended to the knee-joint. He walked with a limp, and examination of the hip-joint showed that the movement of abduction was limited; flexion and

FIG 457 —Right hip-joint when the patient was seen in June, 1934

extension were normal. He was treated with rest in bed, but this had a strangely slight effect upon the pain.

When I first saw him in June, 1934, at the Purley War Memorial Hospital, I noted that the physical signs were strangely disproportionate to the severe pain

which he experienced. He was sent for X-ray report on the right hip-joint with a suggested diagnosis that the condition of the joint was tuberculous, but with the reservation that malignancy must be excluded. I think this alternative was suggested by the severity of the pain and by the fact that this pain was still marked, even though the patient had been resting for a month. The evidence in favour of tuberculosis of the hip was very strong, for the patient had had sanatorium treatment in childhood for tuberculosis of the lungs and mediastinal glands. He had had five children, all of whom had died in infancy from tuberculosis, according to the patient's statement.

Dr. Colyer made the following X-ray report on the right hip: "Large irregular area of rarefaction in bone above and on inner side of acetabulum, with thinning

FIG. 458 —Right hip-joint after death

of bone socket about its centre. The bone surrounding the rarefaction is slightly sclerosed, suggesting an infective condition: tuberculosis is the most probable; does not suggest growth to me." (*Fig.* 457.)

With the assistance of Dr. A. H. Campbell, Tuberculosis Officer to the Surrey County Council, the patient was admitted to the Royal Sea Bathing Hospital, Margate, on June 29, and from that date Dr. B. W. Armstrong, Medical Superintendent, has been good enough to report on his case as follows :—

" On admission the right hip was in a position of slight flexion and adduction. There was a small swelling, (?) abscess, on the anterior surface of the upper thigh; enlarged inguinal glands; local heat; pain on attempted movement but not particularly severe. There were some coarse breath-sounds and areas of increased

vocal resonance in the upper left chest. Clinical evidence of some scattered fibrosis. His temperature was normal or subnormal from the date of his admission to September, when, four days after the patient was fixed in an abduction frame, his temperature rose to 101° and remained about that level for over two months, when it gradually fell and remained subnormal until his death. There was nothing to arouse suspicion of any other diagnosis than tuberculosis, particularly as our radiologist reported that there was chronic pulmonary tuberculosis of the right apex and tuberculosis of the upper part of the acetabulum and ilium above it, with a fair-sized abscess lying lateral to the joint. He was put up in extension, but the infiltration and induration involving the upper part of the thigh increased and he was suffering very severe pain. This was not relieved by an abduction frame, and in the hope of evacuating a deep-seated abscess an aspirating needle
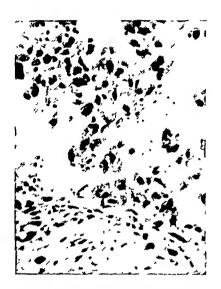
FIG. 459.—Post-mortem section of growth.

was put in the swelling on two occasions without finding pus. On the second occasion a small piece of solid material was sucked into the syringe, which microscopically was reported to be a mixed-celled sarcoma.

"He continued to go downhill and required enormous doses of mòrphia to relieve his pain. The X-ray taken post mortem (*Fig.* 458) shows an extensive destruction of the ilium, which was verified at the autopsy, and there were no secondary deposits discovered in the chest or abdomen."

The Clinical Research Association reported on the small fragment removed by an aspirating needle and on a post-mortem section of the growth that it was a cellular atypical giant-celled sarcoma. Mr. Davies-Colley has been good enough to examine the section, and reports that it shows "the usual polymorphic type of osteogenic sarcoma of bone and suggests a very high degree of malignancy" (*Fig.* 459).

METAPHYSIAL ACLASIS WITH TUBERCULOUS INVOLVEMENT OF A JOINT

BY A. CAMERON ARMSTRONG, LIVERPOOL

THE following case is presented as having two unusual features of interest—namely, the occurrence of tuberculosis in a joint the site of the exostoses typical of metaphysial aclasis, and the extensive involvement of its synovial membrane with tuberculosis without appreciable loss of movement or deformity of the joint, without radiographic bone changes, without pain, and, as far as could be seen at biopsy, without involvement of articular cartilage or bone with the disease. While Hale,[1] in a consideration of 50 cases of metaphysial aclasis, describes tuberculosis as the commonest associated disease, he makes no reference to its special localization

Figs. 460, 461 —Radiographs of left knee showing presence of bony outgrowths (August, 1934)
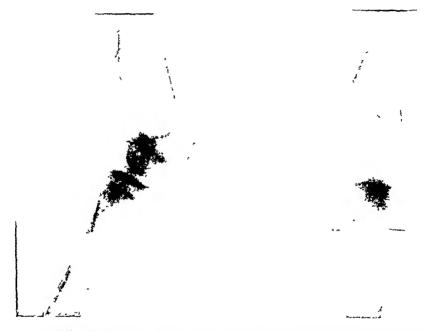
in joints. The hereditary factor which forms such a prominent feature of his cases, and of others, was not obvious in the one here described.

M. M., aged 12, schoolgirl, daughter of working people, first attended for examination on Aug. 23, 1934, stating that the previous day she had noticed a swelling of the left knee, and was experiencing difficulty in getting downstairs. There was no trauma, and no history of infectious disease or other illness. Her general health was said to be good and she was of normal height and weight. There was no history of cough or chest trouble present in any member of the family.

Examination showed a painless effusion into the left knee. The movements of the joint were full, apart from the last few degrees of flexion limited by the

effusion. There was no wasting of the thigh. X-rays of the left knee showed the presence of bony outgrowths characteristic of metaphysial aclasis, but no evidence of tuberculous involvement of the joint (*Figs.* 460, 461). X-rays of the other knee showed a similar condition. Further radiograms of the ankles, wrists, elbows, and hips, showed no abnormality. The urine was normal. The family history contra-indicated congenital syphilis. She was sent to the massage department for quadriceps drill, and the effusion into the knee gradually became less, while the thigh did not waste.

On Oct. 16 there was no effusion, but a definite thickening of the synovial membrane below the patella. This had increased markedly by January, 1935, when she was admitted to hospital. At this time she was anæmic, and not looking

Figs. 462, 463.—Lateral and antero-posterior radiographs of the knee taken in January, 1935.

well. Wassermann and Kahn tests were negative. Further X-rays of the knee at this time (*Figs.* 462, 463) showed no evidence of tuberculosis, as did the X-ray of the chest, but owing to the absence of improvement an arthrotomy was performed, and the synovial membrane of the joint was found to present the characteristic appearance of tuberculous infection. The articular cartilage and the portions of bones that were visible were normal in appearance. Microscopic sections of the synovial membrane confirmed the presence of tuberculosis. A Thomas splint was applied to the limb, and the child made very rapid improvement in her general health. No other member of her family, as far as is known, has a condition of metaphysial aclasis.

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A RETROPERITONEAL ENTEROGENOUS CYST

By LOUIS J. HORN

LATE RESIDENT SURGICAL OFFICER,
GLOUCESTERSHIRE ROYAL INFIRMARY, GLOUCESTER

ENTEROGENOUS cysts, though not extremely rare, are sufficiently so to be worth recording. The following case showed some unusual features as regards form and position of the cyst.

A male child, C. J. B., aged 4, was admitted to the Royal Infirmary, Gloucester, on June 21, 1934, with a history of abdominal pain coming on in spasms, during two of which the child had vomited. The symptoms had been present for twenty-four hours and had become worse after the giving of a dose of castor oil, which had produced several actions of the bowel. There was nothing distinctive about the vomitus or the stools. No history of previous similar attacks was obtainable. The temperature was 98·4° and the pulse 124 per minute.

On examination there was much tenderness and guarding in the region of the right iliac fossa, and some tenderness on rectal examination. A diagnosis of acute appendicitis was made, and the abdomen opened by the McBurney muscle-split incision under ether anæsthesia. There was a moderate amount of pale straw-coloured fluid present in the peritoneal cavity. The appendix was normal, but a sausage-shaped tumour was felt, extending from the mid-pelvis almost to the hepatic flexure of the colon. It was retroperitoneal and lay parallel with and to the right of the ascending colon. The cæcum partly overlapped the tumour, as shown in *Fig.* 464. The incision was then enlarged to the extent of 1 in. in an upward direction and ½ in. in a downward direction. The pelvic end of the cyst was lightly adherent by fresh lymph to the surrounding structures. The peritoneum was incised between cyst and colon, and easily stripped from the former, which was then freed. A flat leash of vessels of supply entering its upper part from beneath the ascending colon was clamped and ligated, and the cyst removed. Beyond some areolar tissue there was no connection of any sort between the cyst and the colon. The child's condition was good at the completion of the operation, and he made an uneventful recovery.

Fig. 464.—Condition found at operation.
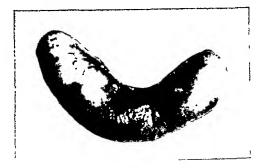
Fig. 465.—Appearance of the cyst after removal

Examination of the cyst showed it to be 7 in. in length, and 2 in. in diameter. It was sausage-shaped (*Fig. 465*) and semi-translucent in appearance. The wall closely resembled that of small intestine, and had well-marked outer longitudinal and inner circular layers of muscle. There was no peristaltic movement visible as has been described in some such cysts after their removal. The cyst was carefully opened at one end, and found to contain clear fluid. A microscopic

Fig. 466.—Microscopic section of the wall of the cyst.

section of the wall and an examination of the fluid were made by Dr. E. N. Davey, pathologist to the institution. The section shows two well-marked muscular layers and a poorly developed or atrophic mucosa (*Fig. 466*). The mucosa shows simple villi covered by columnar epithelium containing numerous goblet cells. The fluid was of low specific gravity, and contained mineral salts and protein, but no intestinal ferments.

COMMENT

Congenital cysts and diverticula are known to occur in practically all parts of the alimentary tract. The greater number of those which have been described reproduce more or less completely the structure of the gut, thus indicating their origin. The type of epithelium may be no guide as to which portion of the gut they came from, since several factors tend to modify this—viz., changes brought about by tension and inflammation, and heteromorphic changes due to the abnormal environment of such epithelium—cf. the common finding of gastric mucosa or

pancreatic tissue in Meckel's diverticula. There are two modes of origin of these cysts which reproduce bowel structure :—

1. Those which arise in connection with some unobliterated portion of the vitello-intestinal tract. There may be a fibrous persistence of this tract, with a cyst along some part of its course. The tract may not be represented along its whole length, but a cyst occur on the antimesenteric border of the gut in the position of the more usual Meckel's diverticulum, or underneath the peritoneum deep to the umbilical scar.

2. Those which arise in connection with diverticula of the developing gut.

The work of Lewis and Thyng[1] in particular throws light on this mode of origin. They examined the developing gut of many rabbit and pig embryos of about 5 to 20 mm. in length. Many of these showed vacuolation and diverticula in the endoderm, especially in the region of the jejunum and ileum. Some of these diverticula were seen to pierce the developing muscularis, and in one pig embryo there was an epithelium-lined cyst outside the muscularis, and a solid cylindrical outgrowth of the gut epithelium adjacent ; connection had been lost between the two. Their researches suggest that these cysts have their origin in this way. It will readily be understood that such a piece of sequestered endoderm may come to occupy almost any position in the abdomen ; either between the layers of the mesentery, or behind the peritoneum. Also, since it has to traverse the muscularis, it may be held up in between any two layers, and develop in that position. This latter is, indeed, a common position in which these cysts are found.

The ileocæcal region is a favourite site for enterogenous cysts ; they are usually intramural, but some are free in the mesentery or retroperitoneal. Cases of so-called reduplication of the bowel have been described. In these is seen a tube or a cyst parallel to the bowel. There may be a communication of the lumina or merely a firm union of the walls ; one or other is usually present, thus indicating that these reduplications are really diverticula that have grown along parallel with the bowel from which they sprung. They are essentially the same as the intramural ones, and those which have become more remote from their parent bowel. These forms are mentioned because the cyst under discussion was elongated in shape, and lay more or less parallel to the colon. It does not, however, I think, enter this category, since it was free of the neighbouring colon, and, both in naked-eye and microscopic structure resembled small intestine. It is, apparently, one that has become farther separated from its source of origin than is usual.

The mild inflammatory state of its lower end probably caused the symptoms and signs, since it doubtless caused an increase of fluid and therefore of tension in the cyst. There was no evidence of obstruction to the bowel by pressure, which is the usual mechanism by which these cysts cause symptoms ; more especially in the case of the intramural ones. Many of them do not cause symptoms at all, but have been found accidentally at autopsy.

I am indebted to Mr. Arnold Alcock for permission to publish this case.

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A CASE OF INTRACRANIAL PNEUMATOCELE

By A. E. PAYNE and W. D. JEANS, Leicester

References in the literature to the presence of air in the cranial cavity as a complication of a fracture of the skull are fairly numerous, but the similar entry of air as the result of the impairment of the integrity of the skull by an osteoma of the orbito-ethmoidal plate is much more rarely recorded, only two previous references having been found in the literature. The first of these is by Harvey Cushing[1] and is described by him as " a large intracranial pneumatocele of unexplained origin exposed and emptied at operation ; recurrence of pneumatocele ; second operation revealing a minute pneumatic sinus alongside an orbito-ethmoidal osteoma ; closure by fascial stamp; recovery ". The second is recorded by F. Gordon Bell,[2] and the condition was first revealed by a highly characteristic X-ray picture, upon which the radiologist, Dr. Barclay, reported : " There is an osteoma arising from the orbital plate of the right frontal bone close to the mid-line and apparently encroaching on the frontal sinus. There is an extensive right pneumocephalus with displacement of the falx and compression of the brain substance. The air probably lies in the subdural space ". The air was found to be in the brain substance at operation, when, as in Cushing's case, the osteoma was successfully removed.

In addition to these two cases Armitage[3] published a somewhat similar case of Cushing's in which there was an osteoma of the frontal sinus with a mucocele communicating with the ventricular system.

Dandy[4] made an exhaustive study of the literature of air inside the skull cavity, which he called pneumocephalus (intracranial pneumatocele or aerocele). All the cases he was able to collect were due either to trauma or to infection (except one case reported by Santoro as being due to a tumour eroding the floor of the skull, but no notes of the case were available) and he says that the condition was due to fracture of the skull affecting the frontal sinus or the ethmoidal or mastoid air-cells, or else due to infection with a gas-producing organism.

He says : " The air may be situated in: (1) the subdural space, (2) the subarachnoid space, (3) the brain, (4) the ventricles, and of these the most common is the intracerebral variety. The entrance of air must occur relatively late, after the dura has become adherent to the traumatized brain, and possibly rupture of the cerebral cortex at the time of injury is also necessary. The anatomy of the frontal region is favourable to the production of intracerebral pneumatocele, first because the dura is so closely applied to the frontal bone that a fracture readily tears the dura, and second because the tip of the frontal lobe is in such close apposition to the dura that the cerebral cortex as well as the meninges is easily ruptured. Even so, it is doubtful if an intracerebral pneumatocele could develop without an added factor, i.e., the increased pressure of air within the cranial sinuses such as is produced by sneezing, coughing, straining or possibly even swallowing."

Our case was that of a gasworks labourer aged 58 years. It was impossible to obtain any history from the man himself, and his relatives could not give a
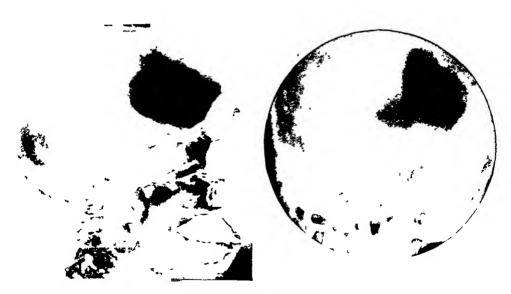
FIG. 467.—The brain taken from above, showing the extent to which the frontal lobe could be collapsed by withdrawing air, and the osteoma below the frontal pole.

FIG. 468.—A section of the brain showing the extent of the cavity and its relation to the caudate nucleus and the internal capsule.

satisfactory detailed account. He had complained of headache (apparently his only complaint) for three years, but was able to follow his occupation until he was knocked down by a bicycle six weeks before admission. He was apparently uninjured by this mishap, but shortly afterwards began to lose his memory for recent events.

ON ADMISSION.—The man was unable to give any account of himself, and was not very co-operative during examination ; he could only answer ' yes ' or ' no ', and then not always in the right context. There was weakness of the whole of the right side of the body, with increase of the deep reflexes on the right side, but with normal plantar responses. It was impossible to test sensation in any way. There were no signs of any increase in intracranial pressure, the fundi being normal and the cerebrospinal fluid pressure being only 70 mm. of water. The cerebrospinal fluid itself showed some change from the normal, cells being increased to 7 per c.c.,

FIGS 469, 470 —X-ray appearances

protein content to 70 mgrm., and the gold curve altered to 1223221000. The report on the skull X-ray said : " The left frontal sinus is occupied by a dense bony mass, and there is a large collection of air in the left frontal region, apparently communicating with the frontal sinus."

OPERATION.—Two days after admission he became gradually unconscious, with a complete right-sided paralysis and a right extensor plantar response. As the coma gradually deepened during the next two days, Mr. Barrett turned down a left frontal flap. The dura was found to be very adherent over the frontal lobe ; the aerocele was aspirated, and the osteoma could then be seen below the collapsed frontal lobe. Owing to the patient's poor condition nothing more could be done, but it was hoped that relief of pressure would procure a return to consciousness. Unfortunately this did not happen and the patient died the following day without any return to consciousness.

POST-MORTEM EXAMINATION.—Autopsy showed an osteoma completely destroying the roof of the left frontal sinus. Immediately above this there was an opening in the dura and in the base of the frontal lobe measuring 1 cm. in diameter. This opening led directly into a cavity measuring 6½ cm. antero-posteriorly, 3 cm. from side to side, and 4 cm. in depth, and stretching back almost as far as the caudate nucleus. (*Figs.* 467, 468.)

Microscopical sections taken from different places along the cavity all showed normal brain tissue ceasing abruptly at the cavity.

The X-ray appearances (*Figs.* 469, 470) are so startling and unexpected that any failure to accept the obvious intrepretation as the right one can be more readily understood than excused, this obvious interpretation being that, not only are the appearances due to a collection of air, but that the air is intracerebral, and neither intraventricular nor subdural. As against the former there is no sign of the normal outlines of any of the ventricles, and as against the latter the position and shape of the collection, especially as viewed in coronal section, are so much those of the cerebral hemisphere itself that an equal wall of brain tissue around it seems certain. That the air is under pressure is evident, and it is the interplay of this pressure and the resistance of the surrounding structures which result in the bulge across the mid-line in the lower part where the restraining influence of the falx is no longer present. At only one part of its containing wall does the collection of air become superficial, and that is the point where the frontal lobe abuts on the frontal sinus. The sinus itself is seen to be completely occupied by a dense osteoma which is tending also to extend into the ethmoid region. The close association of the pathological air-cell with the aerocele could hardly be other than one of cause and effect.

DISCUSSION

The similarity of our case to those described by Cushing, and to that described by Bell, is very striking. It would appear that air may enter the brain substance in one of three ways : (1) By the formation and rupture of a cerebral abscess ; (2) By the formation and discharge of a cerebral mucocele ; (3) By the admission of air through the destruction of the roof of one of the sinuses either by a fracture or by a tumour. In our case the roof of the frontal sinus was completely destroyed and the dura and cerebral cortex were very adherent, both to each other and to the bone. The walls of the cavity in the brain were composed of normal tissue, so that it seems probable that the aerocele was caused by a sudden increase in pressure following nose-blowing or some such other simple procedure, and by a splitting of the brain tissues along the natural layers of cleavage.

The symptomatology and clinical findings in this case were very suggestive of a frontal tumour, and the true diagnosis was only made possible by X rays, which it is very important to employ in the routine investigation of all intracranial conditions.

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A CASE OF RETROGRADE INTUSSUSCEPTION OCCURRING DURING LIFE

By EMLYN E. LEWIS

RESIDENT SURGICAL OFFICER, QUEEN'S HOSPITAL, BIRMINGHAM

A WOMAN, aged 47, was admitted to this hospital on Aug. 30, 1935, with a history of colicky abdominal pains of three days' duration. For twenty-four hours prior to admission she had vomited on a number of occasions. Her bowels had not been opened for three days, neither had she passed flatus. She had noticed increased difficulty with her bowels over the last three months. Her pulse-rate was 120, her temperature subnormal, her abdomen very much distended, especially over the left side, and tympanitic all over. A diagnosis of intestinal obstruction due to volvulus was made.

OPERATION.—On opening the abdomen under spinal anæsthesia, the transverse colon was found to be greatly distended and felt very thickened. This distension and thickening continued back to the cæcum, where the thickening ended in a hardish mass situated at this point. Only a few inches of collapsed pelvic colon could be felt, and on tracing this upwards it was found to enter the gut proximal to it and a few inches distal to the splenic flexure. One realized immediately that this was a retrograde intussusception and that the mass at the cæcum was the apex. The intussusception was reduced by the usual manipulations, some difficulty being experienced in reducing the apex. After reduction, the apex of the intussusception was found to be that part of the pelvic colon opposite the longest portion of the pelvic mesocolon. The apex of the intussusception was gangrenous over about 8 in. The transverse and pelvic colons were markedly elongated, the lumen of the latter being unusually large with its walls very thickened. The pelvic mesocolon, too, was elongated, being about 20 in. long opposite that part of the pelvic colon which formed the apex of the intussusception. The gangrenous loop was treated on the lines of Paul's operation, being delivered on to the abdominal wall via a left iliac incision. The operation was completed by tying a Paul's tube into the gangrenous portion.

SUBSEQUENT HISTORY.—Twenty-four hours after operation the patient's general condition was highly satisfactory and the colostomy was working very well. This remained so until the fourth day, when she developed signs of a right-sided pneumonia, from which she succumbed on the sixth day following operation. Unfortunately a post-mortem examination was refused.

Comment.—The case has been recorded because of the rare condition found at operation. Retrograde intussusceptions are said to occur only in the throes of death, and then as a rule only in the small intestine. Occasionally in life intussusception may take place at a gastro-enterostomy opening. Lockhart-Mummery states, " Retrograde intussusceptions do occur but only during death or as a result of asphyxia; they are not met with in practice." The condition in the case recorded above must have been present for three days at least, and but for the onset of pneumonia the patient would have made a good surgical recovery. At no time was there any evidence of peritonitis.

LEFT DIAPHRAGMATIC HERNIA : PERFORATION OF GASTRIC ULCER INTO LEFT PLEURAL CAVITY

By A. H. SANGSTER, BIRMINGHAM

THE following case is presented more for its pathological interest than for its clinical importance.

James H., a widower, aged 64 years, was admitted to hospital in emergency as a case of perforated gastric ulcer. He gave a history of the sudden onset of acute

Fig. 471.—Condition found post mortem. D, Diaphragm; C, Apex of loop of colon; P, Pericardium.

abdominal pain four hours previously, starting in the left side of the epigastrium and rapidly becoming more widespread. He denied any previous ill health and gave his age wrongly, but was in extreme pain and was confused, having been given morphia by his doctor before admission. Later inquiries, however, showed that he had been in hospital twice before and the diagnosis of diaphragmatic hernia made.

ON EXAMINATION.—The patient appeared a wasted old man in extreme pain with a temperature of 99°; the respirations were very shallow and slow, four per minute. No abnormal sounds were heard in the chest, the heart-sounds were weak and in the normal position, the pulse was imperceptible. The abdomen appeared full with general board-like rigidity.

OPERATION.—His condition failed to improve with $\frac{1}{4}$ gr. of morphia and a heat cradle, so laparotomy was performed half an hour after admission, under general anæsthesia. A left paramedian incision was made and some dirty free fluid evacuated; there was great difficulty in locating the stomach, which was found very high up and overlaid by the transverse colon. The ulcer was found, the perforation being apparently on the posterior surface. The patient's condition became extremely grave and prevented further procedure, so the abdomen was rapidly closed by through-and-through sutures. He died shortly after.

POST-MORTEM EXAMINATION.—Autopsy was performed by Dr. Robinson, who found: General peritonitis; left diaphragmatic hernia; perforation of gastric ulcer into the left pleural cavity; purulent pericarditis; and arteriosclerosis.

The body appeared that of a wasted, grey-haired edentulous man. Fibrinous effusion, 2 pints, containing stomach contents, in left pleural cavity; oval deficiency 8×6 cm. in tendinous portion of left dome of diaphragm, edges smooth and fibrous, no hernial sac. Loop of transverse colon 30 cm. long, stomach with greater curve above and posterior surface forwards, and 25 cm. of dilated jejunum lying in left pleural cavity. Collapse of left lung; loop of colon crossed by fibrous band, 2 cm. broad, running from lower border of left upper lobe to parietal pleura. Fibrinous adhesions between lesser curve of stomach and left border of pericardium; purulent pericarditis with effusion, 3 oz.; perforation, 1 cm. diameter, on anterior aspect of lesser curve of stomach in floor of an ulcer, 3 cm. diameter, lying astride lesser curve 4 cm. from pylorus. Fibrinous peritonitis with turbid effusion, 1 pint; dilatation of jejunum. Phrenic nerve identified running downwards to inner border of hernial orifice, then backwards to œsophageal opening. Congestion and œdema of right lung. Brown atrophy of myocardium; area of fibrosis 2×2 cm. in apex of left ventricle; severe atheroma, especially of coronary arteries. Arteriosclerotic kidneys. Brown atrophy of liver. Remainder of post-mortem showed nothing of importance. (*Fig.* 471.)

REVIEWS AND NOTICES OF BOOKS

The Stomach and Duodenum. By GEORGE B. EUSTERMAN, M.D., F.A.C.P., Head of Section in Division of Medicine, the Mayo Clinic; DONALD C. BALFOUR, M.D. (Tor.), LL.D., F.A.C.S., F.R.A.C.S., Head of Section in Division of Surgery, the Mayo Clinic; and Members of the Staff of the Mayo Clinic and Mayo Foundation. Large 8vo. Pp. 958 + xv, with 436 illustrations. 1935. Philadelphia and London : W. B. Saunders Co. 45s. net.

THOSE who have had the good fortune to visit the Mayo Clinic have realized the vastness of the opportunities there offered for clinical and pathological research upon practically every branch of medical science, and the marvellous organization of team work by which these unique opportunities are utilized to the utmost possible advantage. We heartily welcome, therefore, this monumental work upon the medical and surgical aspects of the stomach and duodenum written by the Heads of the Sections of Medicine and Surgery respectively— two such well-known authors as Dr. Eusterman and Dr. Donald C. Balfour—with the collaboration of thirteen other members of the Mayo Clinic Staff. While founded mainly upon the actual work of the Clinic itself, yet it is evident that an exhaustive search of the literature upon the subject has been carried out and the results incorporated, while every- where full recognition is given to English and foreign investigators. So completely has the ground been covered, and so thoroughly up to date is this volume, that we have failed to find any fact of importance in connection with the stomach and duodenum to which adequate reference has not been made : it is indeed obvious that for a long time this will be the standard work of reference on diseases of these viscera.

A very readable account of the history of these diseases by Dr. Dwight L. Wilbur is followed by a chapter upon the applied physiology of the stomach and duodenum by Dr. Walter C. Alvarez, wherein all the bearings of experimental physiological research upon their functions are considered in a masterly and thoroughly practical manner. Stress is laid upon the act of swallowing, especially of solid food, as being Nature's one big stimulus to peri- stalsis, and it is pointed out that some of the paretic distension of the bowels that occurs after many operations is due to the enforced fasting so often insisted upon. In this connection a sphere of usefulness is found for the American habit of chewing gum. Dr. F. C. Mann, whose fame as an experimental investigator is world-wide, writes fully upon the experimentally produced chronic gastric and duodenal ulcer, and shows that practically every aspect of the formation and healing of these ulcers as met with clinically can be reproduced and studied in the experimental animal. This has entailed an enormous amount of experimental work, the results of which are concisely stated, while some excellent reproductions are given of experi- mentally induced ulcers and their healing.

The section on the surgical pathology of the stomach and duodenum by Dr. W. C. McCarthy details the findings of the careful investigation during the years 1899 to 1933 inclusive of no less than 4129 gastric and 1589 duodenal specimens, all of which were removed during the course of a surgical operation. The subject of ' dyspepsia ' is dealt with most exhaustively under the four headings of ' organic ', ' reflex ' ' systemic ', and ' functional ', and the description of the methods of clinical investigation of the patient indicates the thorough- ness and care with which these examinations are carried out routinely. Gastroscopy by the Wolf-Schindler flexible gastroscope has not yet been generally adopted at the Clinic. At the top of page 142, in referring to Morley's work upon the mechanism of deep tenderness in gastric ulcer, it is stated—" Morley concluded that the tender point was situated in the anterior part of the parietal peritoneum, that is, that it was a true visceral tenderness " : it is obvious that these two statements are incompatible, the first alone correctly stating Morley's opinion. The chapter on roentgenologic diagnosis is excellent and deals not only with the

appearances of the stomach and duodenum in the normal and in diseased states, but describes fully the appearances that are to be regarded as 'normal' after the successful performance of the various surgical operations upon these viscera, and also as 'abnormal' when post-operative complications supervene—e.g., gastrojejunal ulcer.

The subject of duodenal ulcer is discussed thoroughly in all its aspects, and the indications for medical and surgical treatment respectively are most judiciously considered, while each step of the various operative procedures applicable is concisely described and splendidly illustrated. An unusual feature is a chapter on 'duodenitis' as a precursor and as an accompaniment of duodenal ulcer, while in other chapters the rarer lesions of the duodenum—benign and malignant growths, tuberculosis, fistulæ, parasites, diverticula, paraduodenal herniæ, injuries, and foreign bodies—are brought fully up to the present state of our knowledge.

The surgical treatment of gastric ulcer and gastric carcinoma is magnificently described and profusely illustrated, and in no other work can such a complete and excellent account of that very distressing post-operative sequel—anastomotic ulcer—be found. The conclusions arrived at as to its surgical treatment are that if the original duodenal ulcer has healed without producing any obstruction, the operation of choice is disconnection of the anastomosis and nothing more, while, should the ulcer be still active or have produced obstruction, the best course is partial gastrectomy, preferably with union by the Billroth I method. It is a sad reflection upon surgical energy and judgement that it has been found necessary to write a section upon 'gastro-ileostomy' and its sequel in 'ileac ulcer'. Attention is drawn to the almost complete limitation of gastro-jejuno-colic fistula to the male sex, there being but one female out of 74 cases observed at the Mayo Clinic. Post-operative complications are so fully described that it is difficult to conceive of any emergency arising after operation upon the stomach or duodenum that is not fully dealt with in this volume.

Typical diet-sheets for the pre- and post-operative treatment of gastric and duodenal ulcer and gastric carcinoma are given in the appendix.

This volume is thoroughly well calculated to maintain the world-wide and exceedingly high prestige already attained by the Mayo Clinic.

Diseases of the Rectum and Colon and their Surgical Treatment. By J. P. LOCKHART-MUMMERY, M.A., M.B., B.C. Cantab., F.R.C.S., Senior Surgeon to St. Mark's Hospital. Second edition. Large 8vo. Pp. 616 + viii, with 247 illustrations. 1934. London: Baillière, Tindall & Cox. 35s. net.

WE welcome a second edition of this excellent work. A period of eleven years has elapsed since the publication of the first edition, during which time, as the author points out in the preface, considerable advances have been made in our knowledge of the surgery of the rectum and colon. As the result, a large part of the book has been entirely re-written and several new chapters have been added. In addition, ninety new illustrations have been included, chiefly photographic reproductions of the technique of actual operations.

The first part of the book contains chapters on diseases of the rectum and anus; the remainder is devoted to diseased conditions of the colon.

The opening chapter gives a succinct account of the anatomy of the rectum and colon. Then follows an account of the methods of examination of a patient suffering from rectal disease, stress being laid upon the necessity of carrying out an examination by means of the sigmoidoscope in every instance in order to determine whether diseased conditions exist beyond the reach of digital examination. The author's method of preparing a patient for operation and the details of the after-treatment which he adopts are set forth in the succeeding chapter. The subject of hæmorrhoids is fully discussed, the various methods of treatment receiving careful consideration. The technique of Whitehead's operation is described in detail, but the method is not recommended as the results usually obtained by the generality of surgeons are not good. In the following chapter the subject of prolapse of the rectum is dealt with at length and the technique of the author's method is strongly advocated as yielding excellent results. Abscess, fissure in ano, and the various inflammatory processes encountered in the rectum are elaborately discussed. Two chapters are devoted to the subject of fistula and its surgical treatment, much useful information being incorporated therein. The classification of fistula is based upon causation, no mention being made of the relationship of the original

abscess cavity to the muscular and connective-tissue planes in determining the various types that are met with. The author lays great stress upon the effect of division of the external sphincter muscle in the production of an incontinent anus following operations for fistula. In those instances in which the main track passes beneath the muscle he is emphatic in his opinion that the muscle should not be divided at the primary operation, but should be dealt with at a later stage when the greater part of the original wound has healed. As the result of having been extremely careful to avoid injury to the external sphincter he says : " I can confidently assert that, although I have operated for fistula a great many times, I have never produced an incontinent anal opening, and there are no patients of mine walking about this earth cursing their misfortune and my incompetence on this account."

We are constrained to think that such a splendid record is not solely due to the avoidance of division of the external sphincter, because we are not aware that incontinence results from the operation usually adopted for the cure of a fissure which entails complete division of the muscle.

Chapters devoted to the consideration of pruritus ani, rectal pain and neuralgia, simple tumours of the rectum and colon precede a very interesting discussion of precancerous conditions. The author believes that cancer only occurs in those who have inherited a genetic susceptibility to mutation of the cells in certain tissues, and that the susceptibility is to hyper-plasia of the cells. As a result of hyperplasia adenomata are formed which not uncommonly eventuate in cancer. The subject is a fascinating one and well worthy of further investigation. Cancer of the rectum is elaborately discussed from the etiological, symptomatological, patho-logical, and surgical points of view. When describing the methods of extension of rectal growths, the impression is conveyed that the determination of the three paths of spread, namely, (1) by infiltration of surrounding parts through continuity of tissue, both on the surface and deep to it, (2) by the lymphatics, (3) by the veins, was due to an investigation carried out in the Cancer Research Department of St. Mark's Hospital by Dr. Cuthbert Dukes and reported by him in an article entitled " The Spread of Cancer of the Rectum " which appeared in the BRITISH JOURNAL OF SURGERY in 1930. It seems to be within our recollection, however, that these modes of spread were originally described in a paper read in the Section of Surgery at the Annual Meeting of the British Medical Association held at Cambridge on July 1, 1920, and which was published in the *British Medical Journal* of Nov. 13 of that year.

The remainder of the book is concerned with abnormalities and diseases of the colon and their treatment.

We have pleasure in commending the book as representing the opinions of one who has spent many years in the practice of rectal surgery.

An Introduction to Surgery. By RUTHERFORD MORISON, M.D., F.R.C.S. (Edin.), F.R.C.S. (Eng.), M.A., D.C.L., LL.D., Emeritus Professor Surgery, Durham University; and CHARLES F. M. SAINT, C.B.E., M.D., M.B., F.R.C.S., F.R.A.C.S., Professor of Surgery, Cape Town University. Third edition. Demy 8vo. Pp. 367 + xii, with 231 illustrations. 1935. Bristol : John Wright & Sons Ltd. 15s. net.

PROFESSOR RUTHERFORD MORISON'S name is in itself a sufficient recommendation, but the appearance of the third edition is additional evidence of the usefulness of this book. The careful perusal of its pages, however, must arouse in the reader's mind certain criticisms and doubts with regard to the ideal method of presenting fundamental principles to the student beginning the study of surgery. When allowances have been made for the opinions of indi-vidual teachers, it must be admitted that any sound system should state the principles so clearly that the ideas conveyed to the student may be entirely free from ambiguity or confusion, that details should be introduced only to help to clarify these ideas, and that no error of terminology or fact should be permitted.

If the present volume is examined by this standard, it must be confessed that though an attempt has been made to simplify the work of the student by asking him to regard all pathological processes as " part of an all-embracing whole ", the result is more closely akin to abstract philosophy than to the craft or even to the science of surgery. As the natural outcome of this system of unification, we are asked to regard an acute abscess as a spherical acute ulcer, and a sinus as a tubular ulcer, while syphilis, tuberculosis, and malignant disease

are grouped together in one chapter because of their close resemblance to one another. Though it is of fundamental importance to show that tissues respond to any kind of injury in a similar fashion, to infer that the variations in this response are so slight that all disease processes are identical is a hindrance rather than a help to the beginner.

Expressions of opinion are in many instances presented as statements of fact, there are several errors in terminology, more particularly in reference to malignant disease, and much of the detail is unnecessarily burdensome in a volume such as this. It may be that the authors have felt the necessity for including these minor points so that the book may compete with other short text-books on surgery for examination purposes, but it is regrettable that they should have been forced thereby to run the risk of obscuring the principles which it has been their chief object to enunciate.

The Modern Treatment of Burns and Scalds. By PHILIP H. MITCHINER, M.D., M.S. (Lond.), F.R.C.S., Hon. Surgeon to H.M. the King, etc. Crown 8vo. Pp. 64 + x, with 12 plates. 1935. London: Baillière, Tindall & Cox. 5s. net.

THIS admirable little book states with military precision how burns of all varieties should be treated. Its practical value is so great that it should be carefully studied by every medical student and practitioner, and its precepts should be drilled into all those responsible for first-aid treatment, especially in industrial establishments. As Mr. Mitchiner points out, there has been a tendency in the past to regard burns and scalds as of minor importance in surgery, but there is now no excuse for perpetuating the evil effects of this attitude towards injuries the mortality-rate of which can be reduced tenfold by proper methods of treatment.

Though the principal object of this book is to set forth these methods, a brief but adequate description is given of the pathological processes resulting from burns and scalds, and the superiority of a 2 per cent solution of tannic acid in water over all other local applications is explained on theoretical grounds as well as being proved by experience. Why 2 per cent is preferable to a stronger solution, the reason for the inclusion of perchloride of mercury in the formulæ for powders and tablets, and many similar practical questions, are fully considered, and the hints with regard to burns resulting from special agents, such as electricity, tar, cordite, petrol, phosgene, and mustard gas, are invaluable. Another evidence of the author's careful attention to detail is the table showing the doses of opium and morphia suitable for children and adults of all ages—a matter which is referred to rather vaguely in most text-books. Mr. Mitchiner has given much attention to the illustrations, which are very helpful, and for which the publishers also deserve a share of the praise.

Urology in General Practice. By ALEX. E. ROCHE, M.A., M.D., M.Ch. (Camb.), F.R.C.S., Assistant Genito-Urinary Surgeon, West London Hospital, etc. Demy 8vo. Pp. 356 + x, with 43 illustrations. 1935. London: H. K. Lewis & Co. Ltd. 17s. 6d. net.

THE late General Booth exclaimed, "Why should the devil have all the best tunes?" We might echo, "Why should writings on scientific subjects be so often dry as dust and repellent to even the eager reader"? That erudition is not of necessity allied with dullness has been shown by Huxley in the last century and more recently by Bland-Sutton, Moynihan, and Sir Arthur Keith.

Mr. Roche, perhaps influenced by these writers, has shown that the careful choice of words and the use of a well-restrained humour is not incompatible with a thorough knowledge of urology, and the result has been a most attractive and readable book. The one exception we take, though it may seem ungrateful after reading the book with such pleasure, is that the approach to the subject is that of the surgeon rather than that of the general practitioner; the latter might feel puzzled to find only eleven pages devoted to the study of the enlarged prostate, whilst no fewer than thirty-seven are filled with a discussion—a very able one, we admit—of torsion of the spermatic cord and of the hydatid of Morgagni. Whilst every general practitioner will see many cases of the former, he will be lucky if he sees more than one of the latter during the course of his career. The explanation is, of course, that

Mr. Roche has taken an enthusiastic interest in intrascrotal disease and has written much on this subject; moreover, he partially disarms the critic by his remark that the length of the chapters is not in proportion to the importance of the subjects discussed therein.

The chapters on "The Examination of a Urological Case", on "Hæmaturia and Dysuria", and on "Cystoscopy and Pyelography" are all admirable; so is that on "Urethral Catheters", though we feel surprised that a disciple of Sir John Thomson-Walker should advocate the use of tape for tying in a catheter; we thought that Thomson-Walker's rubber bridle had quite displaced this method as being clean and easier to adjust.

The author emphasizes his points by illustrative cases and by quotations; one of the most delightful of these is the *bon mot* of the physician who visited a ward of prostatic cases and remarked that he thought "many of them would stand a shave and hair-cut if it were done in two stages"; surely (to quote from Mr. Roche's favourite poet), "what oft was thought, but ne'er so well expressed", and a flattering unction to the souls of those surgeons who have encountered undeserved misfortune after prostatectomy.

We commend this book to those of our readers who wish to feel that they are keeping their knowledge of urology up to date, and like a volume that they can read with comfort in the train.

A Text-book of Fractures and Dislocations. Covering their Pathology, Diagnosis, and Treatment. By KELLOGG SPEED, S.B., M.D., F.A.C.S., Professor of Clinical Surgery, Rush Medical College of the University of Chicago. Third edition. Royal 8vo. Pp. 1000, with 1042 illustrations. 1935. London: Henry Kimpton. 50s. net.

THIS treatise on fractures has now earned a well-deserved reputation both in America and this country for its lucid and comprehensive description of this section of traumatic surgery. It opens with two chapters on the general principles of treatment and on operative treatment. These are perhaps the most valuable in the book, as they represent such a sound view of modern methods, accepting and describing all proved advances but not advocating any 'fads'. The detailed description of the first-aid outfit and the teaching by posters and slogans are very practical.

The bulk of the book is concerned with the description of individual fractures and dislocations and their treatment, with a great wealth of excellent illustrations, so that it forms an invaluable book of reference. In the matter of the use of unpadded plaster, of early active movements, and of the danger of applying massage in the early days, the author is not a follower of Böhler's teaching. For instance, spinal fractures are to be nursed for four to eight weeks in bed in hyperextension, and the importance of early active movements is not stressed. And in Colles's fracture the figure shows the hand in palmar flexion, and the splint is to be removed on the second or third day for movements and massage. In the same way Pott's fracture has the plaster case removed after three to four days and routine early walking is not advised. The treatise gives so many methods of treatment that the student lacks a clear guidance as to which to use in any given case.

Wilhelm Conrad Röntgen and the Early History of the Roentgen Rays. By OTTO GLASSER, Cleveland Clinic Foundation. Crown 4to. Pp. 494 + xii, with 94 illustrations. 1935. London: John Bale, Sons & Danielsson, Ltd. 32s. 6d. net.

THE appearance of this book ten years after Röntgen's death serves as a very timely reminder to the modern generation of the wonders of his discovery. Radiology has now taken such a dominating place in medical science that it is well to be able to look back and trace the development of this marvel.

Röntgen was born in Lennap in 1845, the son of a cloth merchant. His early student career was not particularly brilliant, and the facts that he was expelled from school (for refusing to inform about a misdemeanant) and that he failed in his 'Absolutorium' examination gave no promise of a great future. But when once he had devoted himself to pure physics, his industry and accuracy of observation soon gave him both reward and opportunity. Privat-docent at Strassburg, Professor of Physics at Giessen, then at Würzburg (1888), and finally at Munich (1901), were the posts which he filled.

It was on Nov. 8, 1895, that, working alone in his laboratory in Würzburg, he first observed the new rays from the illumination of some crystals of barium platino-cyanide by a Crookes tube which was covered with black paper. He published his discovery to the world on Dec. 18, 1895, in a preliminary communication, which he amplified early in the next year. There probably has never been a discovery which was more quickly acclaimed and appreciated all over the civilized world.

This book tells us the full story and also gives personal notes of this great scientist who combined in himself enthusiasm, industry, and modesty. There is also a complete account of the reception of the discovery by scientists and by the press both lay and medical. It concludes with a bibliography of 1044 references, a very large proportion of which were published in 1896.

The book is delightfully written in English and gives a good biographical sketch of the man and a lucid account of the genesis and growth of his discovery. We think, however, that its value would be increased if some chapters were added on the later development of radiology, whilst a good deal of the detailed repetitions of the early work might be omitted.

Röntgenology: the Borderland of the Normal and Early Pathological in the Skiagram. By ALBAN KÖHLER (Wiesbaden). Translated by ARTHUR TURNBULL, M.A., B.Sc., M.B., Ch.B. (Glasg.), Ex-Demonstrator of Anatomy, University of Glasgow. 7 in. × 10 in. Pp. 682 + xvi, with over 400 illustrations. 1935. London: Baillière, Tindall & Cox. 50s. net.

THE phrase ' German thoroughness ' may perhaps be somewhat hackneyed, but one cannot avoid using this expression to describe one of the main characteristics of this unusually fine piece of work. The book is already familiar to English readers, the first English edition having appeared in 1928, thanks to the able efforts of Mr. Turnbull and others. It is a veritable mine of information, and its scope is well defined in the sub-title, " The Borderlands of the Normal and Early Pathological in the Skiagram."

In this new English edition the general arrangement has not been altered, but the subject matter has been suitably revised and expanded, and many references, together with frequent full summaries of the recent literature, are included. The author relies very largely upon clear line drawings to illustrate his points, although the number of actual skiagrams reproduced is considerable. In the course of the study of radiograms of the various parts of the body in large numbers of subjects, slight variations from what is generally considered the normal are constantly being encountered, and Professor Köhler's work can always be relied upon to solve such problems. In fact, to quote from Professor Fraser's remarks in his Preface, " it is difficult to conceive of any abnormality, or early pathological change demonstrable by X-ray, which is not considered in this excellent Treatise." It can be truly described as an authoritative and standard work, and, considering the enormous part played by radiography in medicine to-day, radiologists, physicians and surgeons, medico-legal experts, and students, should be eternally grateful to the author and the translator for making this volume available in the English language.

The Radiology of Bones and Joints. By JAMES F. BRAILSFORD, M.D. (B'ham.), M.R.C.S., Hunterian Professor, R.C.S., England, 1934-5 ; First President of the British Association of Radiologists, etc. Second Edition. Crown 4to. Pp. 57 + xxiii, with 340 illustrations. 1935. London: J. & A. Churchill Ltd. 30s. net.

THE production of the second edition following so quickly upon the issue of the first one is indicative of the very deserving success of this book. The present edition contains some additions in the text and illustrations, and the index has been reconstructed. There is a very complete discussion upon osteochondritis, voicing the many opinions which have been expressed concerning this subject, and the author has given his own conclusions based upon a very considerable experience. It is probable that the last word has yet to be written on this interesting subject. The section dealing with spondylolisthesis has been reconstructed and rendered

even more informative than it was in the previous edition. The chapter on bone dystrophies has been re-written and brought up to date. A brief description of dental radiology has been included, but it is very incomplete and does not compare at all favourably with the profundity of the rest of the book.

Dr. Brailsford has earned the gratitude of his fellow radiologists and deserves full praise for his very fine work.

The Theory and Practice of Anæsthesia. By M. D. Nosworthy, M.A., M.D., B.Ch. (Cantab.), Anæsthetist to Westminster Hospital, etc., with a Foreword by I. W. Magill, M.B., B.Ch. (Belfast), Anæsthetist to Westminster Hospital, etc. Crown 8vo. Pp. 223, with 35 illustrations. 1935. London : Hutchinson Scientific. 12s. 6d. net.

Dr. Nosworthy's large experience as an instructor in anæsthesia has enabled him to produce this book, which must prove a valuable guide to the novice, and, incidentally, contains much of real interest for the more experienced administrator.

While admitting that the administration of anæsthetics is largely an art, the author insists on the need for an insight into the scientific data upon which judgement may be based, and he describes at some length the recent views on the functions of oxygen and carbon dioxide in human physiology. Four chapters are devoted to theory, and the remaining twelve chapters to clinical material, with special attention paid to modern methods, the descriptions of technique being illustrated where necessary. Among the more recent developments the subject of premedication is described, with useful accounts of the various drugs in common use and the reason for selecting different drugs in particular cases. There obviously is not space in a book of this size to give details of the many ways in which regional anæsthesia may be employed, but under this heading is included a carefully written chapter on spinal anæsthesia, which should convince the reader of the care necessary if accidents are to be avoided and reliable results obtained.

The book cannot fail to become popular, and its readers will realize that the subject matter has been carefully digested and presented to them in an easily assimilable form. A feature of this little work is the thoroughness with which references have been quoted, also the clearness of the type and the neat style in which it has been produced.

A Guide to the Surgical Paper : With Questions and Answers. By R. J. McNeill Love, M.S. (Lond.), F.R.C.S., Surgeon, Royal Northern and Metropolitan Hospitals, etc. F'cap 8vo. Pp. 78. 1935. London : H. K. Lewis & Co. Ltd. 5s. net.

Mr. McNeill Love's small book will no doubt help many people. The plan on which it is founded is ingenious, and while it necessarily covers only a small proportion of the possible questions that may be set, it gives the candidate a scheme on which he may build up an answer to any parallel question. The published answers are necessarily condensed, and lists are made more use of than they should be in the ideal answer, but this book is to be commended, for one knows there is a type of candidate, by no means infrequent, to whom such a guide will be of the greatest possible assistance.

A Text-book of Surgical Pathology. By Charles F. Illingworth, M.D., F.R.C.S. (Ed.), Lecturer in Clinical Surgery, University of Edinburgh, Senior Assistant Surgeon, Edinburgh Western Hospital ; and Bruce M. Dick, M.B., F.R.C.S.(Ed.), Lecturer in Clinical Surgery, University of Edinburgh, Assistant Surgeon, Edinburgh Western Hospital. Second edition. Royal 8vo. Pp. 719 + x, with 301 illustrations. 1935. London : J. & A. Churchill Ltd. 36s. net.

The authors set before themselves the task of writing a book on the pathology of surgical diseases on those aspects which are outside the scope of text-books on general pathology. In this object they have certainly succeeded, as is shown by the fact that the first edition of 1932 has been so soon followed by a second. There will be those who will doubt whether the necessary space should have been available for the introduction of paragraphs upon rare

conditions added to this edition, but there will be only one opinion upon the usefulness of re-writing certain sections. The authors certainly avoid the usual pitfall of clinicians when they undertake to write a volume of this nature on pathology—who mostly forget that their aim is pathology and not clinical surgery. The majority of the illustrations are well chosen and well produced, and the whole of the book is worthy of the house from which it emanates.

Diseases of the Liver, Gall Bladder, Ducts and Pancreas: their Diagnosis and Treatment. By SAMUEL WEISS, M.D., F.A.C.P., Clinical Professor of Gastroenterology, New York Polyclinic Medical School and Hospital, etc. With a chapter by J. P. GRANT, M.D., F.A.C.S., M.R.C.S., and A. J. QUIMBY, M.D., F.A.C.R. Imperial 8vo. Pp. 1099 + xxviii, with 358 illustrations and 6 coloured plates. 1935. New York: Paul B. Hoeber Inc. $10.00.

THE bulk of this large volume will be of more interest to the physician than the surgeon, and to the general practitioner rather than to either. It sets out to deal exhaustively with the practical side of biliary and pancreatic diseases. The chapter on surgery is limited to thirty-seven pages and deals with the preparation of the patient before operation, the standardized operations of cholecystostomy and cholecystectomy, and the removal of stones from the biliary ducts. At the end of the book is a bibliography running into close on 100 pages.

Surgical Nursing and After-treatment. A Handbook for Nurses and Others. By H. C. RUTHERFORD DARLING, M.D., M.S. (Lond.), F.R.C.S. (Eng.), F.R.F.P.S. (Glasgow), Surgeon, Prince Henry Hospital, New South Wales Hospital (Langton Clinic), etc. Crown 8vo. Pp. 738 + xii, with 187 illustrations. 1935. London: J. & A. Churchill Ltd. 9s. net.

THE higher examination standard now required for nurses is well met by this text-book, which at first sight, with its 738 pages, seems unnecessarily formidable. However, it reads clearly and simply, and not only gives the detailed technique of ordinary surgical nursing procedures but also seeks to elucidate them by giving an insight into surgical pathology and operative procedures and complications which may arise therefrom.

The illustrations are numerous and helpful, and the essentially practical nature of the whole book makes it suitable, not only as a guide to nurses in training, but also as a book of reference to those out of touch with hospital practice after their training is finished.

A Text-book of Surgery for Dental Students. By G. PERCIVAL MILLS, M.B., B.S. (Lond.), F.R.C.S., Hon. Surgeon, General Hospital, Birmingham, etc.; and HUMPHREY HUMPHREYS, O.B.E., M.C., T.D., K.H.P., M.B., Ch.B., M.D.S. (Birm), L.D.S. (Eng.), Lecturer on Dental Anatomy, Birmingham University, etc. Fourth edition. Large 8vo. Pp. 342 + xii, with 63 illustrations. 1935. London: Edward Arnold & Co. 14s. net.

THIS book has proved its utility and popularity by the fact that it is now in its fourth edition. It gives a clear account of general surgical principles and of the special surgery of the mouth, jaws, and cranial and cervical regions. The illustrations, though not very numerous, are clear, and the book gives just what dental students require for their examination in surgery.

Estudos cirurgicos (First Series). By ENRICO BRANCO RIBEIRO (Santa Catharina). Large 8vo. Pp. 241. Illustrated. 1934. Sao Paulo, Brasil: Sociedade Editora Medica Limitada. No price given.

THE author dedicates his surgical studies to his teacher, Professor Montenegro. The subjects cover a wide field of general surgery, and show not only that the author is well read in the literature of the world, but that he has original views and is prepared to put them into execution. For example, in dealing with perforation of typhoid ulcers, he has found

it better to do a bold cæcostomy at the conclusion of his suturing operation rather than the ileostomy which is in favour in South America, and he describes his own technique for its performance. He has something to say about such different matters as the origin of gall-stones, the method of dealing with infections of the upper urinary tract, the proper management of cases of ovarian cyst, injuries to the skull involving the meninges, treatment of suppuration by vaccines, neurofibromatosis, cancer of the gall-bladder, and torsion of the spermatic cord. He gives an account of the construction and working of an emergency hospital provided by a power company for its very large list of employees. Altogether the book gives an interesting account of the work of an up-to-date surgeon in Brazil.

Diseases of the Thyroid Gland. By A. E. HERTZLER, M.D., Professor of Surgery, University of Kansas. Third edition. Royal 8vo. Pp. 348. Illustrated. 1935. London: Henry Kimpton. 32s. net.

THE author states that several new factors have intervened since the last edition was published. These chiefly concern the importance of goitre in connection with disease of the heart. He concludes that disease of the thyroid gland is often a continuous process, ending in cardiac death, and says that his experience leads him more and more to remove the whole gland in certain selected cases.

Anatomia della Lussazione congenita del' Anca. By V. PUTTI, Bologna. Pp. 334, with 77 plates, many in colour. Bologna: Licinio Cappelli. Lir. 300.

THIS is a very beautiful atlas, illustrating every phase of the anatomy of congenital dislocation of the hip. The figures, which are of great artistic merit, are drawings, photographs, and X-rays, and are made from dissections as well as from patients.

It would seem that the author, having by his work and experience become the greatest living authority on this subject, has set out to produce the most complete and perfect anatomical description and illustration. In this he has been eminently successful, and we can only express the wish that it may soon be translated into English and also that it may be followed by a companion volume dealing with the clinical aspect of this deformity.

Localized Rarefying Conditions of Bone. As exemplified by Legg-Perthes' Disease. Osgood-Schlatter's Disease, Kümmell's Disease and Related Conditions. By E. S. J, KING, M.D., D.Sc., M.S. (Melb.), F.R.C.S., F.R.A.C.S., Surgeon to Out-patients, Melbourne Hospital. Medium 8vo. Pp. 400 + xii, with 70 illustrations. 1935. London: Edward Arnold & Co. 35s. net.

THIS is a comprehensive monograph containing the most complete account yet published of the various types of osteochondritis juvenilis, post-traumatic rarefaction of bone, and the condition known as osteochondritis dissecans. It embodies the Jacksonian Prize Essay for 1933. As a work of reference it is invaluable. Our only criticism is that the author has perhaps tended to submerge his personal views on the etiology of the conditions, and that the introductory chapter on the structure, development, and physiology of bone is rather too episodic to be easily understood by the tyro. The illustrations, which come from the author's own collection, have been well chosen, and for the exhaustive list of references all surgeons will be grateful.

Bassini's Operation for the Radical Treatment of Inguinal Hernia. By Prof. ATTILIO CATTERINA, University of Genoa. Obl. Imperial 4to. Pp. 58, with 16 coloured plates by Orazio Gaigher, M.D. 1934. London: H. K. Lewis & Co. Ltd. 30s. net.

AN English edition of this atlas of plates illustrating Bassini's operation has been added to the already existing Italian, German, and French publications. For a full account of the work, readers are referred to the review of the German edition which appeared in this JOURNAL for January, 1934 (p. 555).

Collected Papers of St. Mark's Hospital, London: including a History of the Hospital. Centenary Volume, 1835–1935. Compiled by the Medical Committee. Crown 4to. Pp. 440 + xxvi, with 96 illustrations. 1935. London: H. K. Lewis & Co. Ltd. 30s. net.

It was a happy thought that prompted the members of the Medical Committee of St. Mark's Hospital to commemorate the centenary of the hospital by publishing in book form a selection of the writings of past and present members of the staff. A glance at the voluminous contributions to the subject of diseases of the anus and rectum, which is to be found at the end of the book, shows how difficult it must have been to make the necessary selection. We congratulate the Medical Committee on having made an excellent choice, which is not only representative of the progress made in the treatment of rectal diseases throughout the century of the Hospital's existence, but is also indicative of the evolution of the present-day teaching at St. Mark's.

St. Bartholomew's Hospital Reports. Edited by Lord Horder, W. G. Ball, R. G. Canti, C. F. Harris, W. Shaw, H. H. Woollard, R. C. Elmslie, G. Evans, and J. P. Ross. Vol. LXVIII. Demy 8vo. Pp. 351 + xxvi. Illustrated. 1935. London: John Murray. 21s. net.

Following the practice which has been customary in their recent issues, this volume of the Saint Bartholomew's Reports for 1935 contains a series of papers on the urinary tract, particular attention being paid to infections. In these, Mr. Boyd's article on the anatomy and physiology of the kidney is most instructive. Mr. Girling Ball's contribution is a most comprehensive paper on the surgical aspect of the question, which is also dealt with in relation to pregnancy and in other aspects. Mr. Joseph Cunning contributes a sympathetic notice of the late F. A. Rose.

Reminiscences. By Agnes Hunt, D.B.E., R.R.C. Demy 8vo. Pp. 137. Illustrated. 1935. Shrewsbury: Wilding & Son Ltd. 5s. net.

This racy little book, which is introduced by a Foreword by the Hon. Sir Arthur Stanley, is both a delight and a disappointment. A delight because of the breezy and unconventional narrative of travel and adventure, voyages round the world, and a struggle with an early settler's difficulties in Australia. A disappointment because it gives such a meagre account of the great work which Dame Agnes Hunt began before the war, for the cure of various crippling conditions. Herself a life-long cripple, her wonderful pluck and enterprise will always prove that those who are physically handicapped can nevertheless do a great work for the betterment of the world.

Kleine Chirurgie. By Prof. Dr. Hans Kurtzahn. Third edition. Pp. 456, with 169 illustrations. Berlin and Vienna: Urban & Schwarzenberg. 1935. Paper covers, RM. 12; bound, RM. 13.50.

This is a book for the German student, dealing with minor and practical surgery. It is not likely to interest English students deeply.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest for our readers.]

Krebsproblem und praktische Chirurgie. By Prof. Dr. FRITZ KÖNIG (Wurzburg). Part 4 of *Vorträge aus der praktischen Chirurgie*, edited by Prof. Dr. ERICH LEXER (Munich). Royal 8vo. Pp. 27. 1935. Stuttgart: Ferdinand Enke. RM. 1.60.

Die Chirurgie der Hirngeschwülste. By Prof. Dr. N. GULEKE, Direktor der Chirurgischen, Univ.-Klinik, Jena. Part 5 of *Vorträge aus der praktischen Chirurgie*, edited by Prof. Dr. ERICH LEXER (Munich). Royal 8vo. Pp. 40. 1936. Stuttgart: Ferdinand Enke. RM. 2.20.

Der Schenkelhalsbruch: ein mechanisches Problem. By Dr. FRIEDRICH PAUWELS (Aachen). Royal 8vo. Pp. 157, with 186 illustrations. 1935. Stuttgart: Ferdinand Enke. Paper covers, RM. 13.60; bound, RM. 15.00.

Brain Preparations by Means of Defibrillation or Blunt Dissection. By Dr. J. WILH. HULKRANTZ, Professor of Anatomy, University of Uppsala, Sweden. Translated from the first German edition by HERBERT J. WILKINSON, Professor of Anatomy, University of Adelaide. Crown 4to. Pp. 48 + ix, with 48 illustrations. 1935. London: William Heinemann Medical Books Ltd. 10s. 6d. net.

Demonstrations of Physical Signs in Clinical Surgery. By HAMILTON BAILEY, F.R.C.S., Surgeon, Royal Northern Hospital, London, etc. Fifth edition. Large 8vo. Pp. 287 + xii, with 341 illustrations. 1935. Bristol: John Wright & Sons Ltd. 21s. net.

The Early Diagnosis of Malignant Disease. By GEOFFREY KEYNES, M.A., M.D. (Cantab.), F.R.C.S., Assistant Surgeon to St. Bartholomew's Hospital, etc. F'cap 8vo. Pp. 70. 1935. London: John Bale, Sons & Danielsson, Ltd. 2s. 6d. net.

Tumours of the Urinary Bladder. By EDWIN BEER, M.D., F.A.C.S., Visiting Surgeon, Mt. Sinai Hospital; Consulting Surgeon, Bellevue Hospital, New York City. Large 8vo. Pp. 166 + vi, with 52 illustrations (8 in colour). 1925. London: Baillière, Tindall & Cox. 16s. net.

The Early Diagnosis of the Acute Abdomen. By ZACHARY COPE, B.A., M.D., M.S. (Lond.), F.R.C.S., Surgeon to St. Mary's Hospital, Paddington, etc. Seventh edition. Medium 8vo. Pp. 254 + xiv, with 33 illustrations. 1935. London: Humphrey Milford, Oxford University Press. 10s. 6d. net.

Chirurgische Operationslehre. By Dr. MAX SAEGESSAR, Privatdozent an der Universität Bern. Crown 8vo. Pp. 189 + vi, with 132 illustrations. 1935. Berlin: Julius Springer. Paper covers, RM. 7.50; bound, 8.60.

The Principles and Practice of X-ray Therapy. By FFRANGCON ROBERTS, M.A., M.D. (Cantab.), M.R.C.P. (Lond.), D.M.R.E. (Cantab.), Physician in Charge of the Douty X-ray Clinic, Addenbrooke's Hospital, Cambridge. Demy 8vo. Pp. 214 + xii, with 110 illustrations, including 6 plates. 1936. London: H. K. Lewis & Co. Ltd. 10s. 6d. net.

The Foot. By NORMAN C. LAKE, M.D., M.S. (Lond.), F.R.C.S., Senior Surgeon and Lecturer on Surgery, Charing Cross Hospital. Large 8vo. Pp. 330 + vii, with 95 illustrations. 1935. London: Baillière, Tindall & Cox. 12s. 6d. net.

Post-graduate Surgery. Edited by RODNEY MAINGOT, F.R.C.S., Senior Surgeon to the Royal Waterloo Hospital, etc. With an Introduction by the Right Hon. LORD MOYNIHAN OF LEEDS, K.C.M.G., C.B., M.S., F.R.C.S. In three volumes. Royal 8vo. Vol. I: Pp. 1742 + xvi, with 846 illustrations. 1936. London: Medical Publications Ltd. £6 6s. the set, or £2 10s. per volume.

IPSISSIMA VERBA

By Sir D'Arcy Power, K.B.E., London

IX. REID'S BASE LINE

Much good work was being done on the brain in England between 1870 and 1890. Ferrier and Yeo were localizing the functions of the cortex by experimental methods; Schafer as an histologist was tracing the course of the fibres and tracts; Reid as an anatomist was giving surgeons a guide for operating; Macewen, Victor Horsley, Ballance, and Rickman Godlee were operating.

Professor Reid published his communication in *The Lancet* (1884, ii, 539) under the title, "Observations on the Relation of the Principal Fissures and Convolutions of the Cerebrum to the Outer Surface of the Scalp". He was then Lecturer on Anatomy in the Medical School of St. Thomas's Hospital, and is now Emeritus Regius Professor of Anatomy at Aberdeen, and Honorary Curator of the University Anthropological Museum, of which he was the Founder. A Reid Lectureship in Anthropology was founded in his honour at Aberdeen University in 1934, and the first lecture was given by him on December 3, 1934. The portrait which he very kindly sent at my request was taken in 1889, the year he left London for Aberdeen. He says in the article referred to above :—

"What I propose to do is to show that by taking large and easily felt landmarks on the head, and drawing from these certain lines, these lines will indicate accurately enough for all practical purposes the position of the principal sulci, and that by removing in any of these lines a piece of the scalp and skull an inch square, or by applying the one inch trephine to the skull, with the centre pin on the line, we can expose the fissure in any part of its course.

"The landmarks which can be easily felt on the outside of the scalp, and with reference to which lines can be drawn to indicate the position of the sulci are the glabella, or depression between the two nasal eminences, just above the root of the nose, external occipital protuberance, superior curved line of the occipital bone, parietal eminence, posterior border of the mastoid process, depression just in front of the external auditory meatus, external angular process of the frontal bone, frontal part of the temporal ridge and the supra-orbital notch. We shall also suppose that the Base line (*see Figure*), from which all perpendicular lines are drawn, runs through the lowest part of the infra-orbital margin and the middle of the external auditory meatus."

The line is not further defined in the text, but it soon passed into common use as 'Reid's base line' and was serviceable to several generations of surgeons as a rallying point when small trephines were used, osteoplastic flaps had not been thought of, and operations were limited to the cortex. It is now more of historical interest than of practical value. Reid continues :—

PROFESSOR REID

" *Transverse Fissure*.—This is indicated by drawing a line along the superior curved line of the occipital bone from the external occipital protuberance to the external auditory meatus—that is, along the line of junction of the head with the neck posteriorly.

" *Fissure of Sylvius*.—To find this draw a line from a point one inch and a quarter behind the external angular process of the frontal bone to a point three-quarters of an inch below the most prominent part of the parietal eminence. Measuring from before backwards, the first three-quarters of an inch of the line will represent the main fissure, and the rest of the line will indicate the horizontal

limb. The ascending limb will start from the posterior end of the line indicating the main fissure—that is, two inches behind and slightly above the external angular process—and run vertically upwards for about an inch (*see Figure*).

"*Fissure of Rolando*.—To find this, and at the same time the region of the ascending frontal and parietal convolutions, first indicate on the surface of the scalp the longitudinal fissure and the horizontal limb of the fissure of Sylvius, next, from the base line draw two perpendicular lines to the top of the cranium, one (DE) from the depression in front of the external auditory meatus, and another (FG) from the posterior border of the mastoid process at its root. We shall then have described on the surface of the head a four-sided figure, bounded above and below by the lines for the longitudinal fissure and horizontal limb of the fissure of Sylvius respectively, and in front and behind by the two perpendicular lines. If we now draw a diagonal line (FH) from the posterior superior angle to the anterior inferior angle of the space, this diagonal line will lie over the fissure of Rolando. In the majority of cases the fissure of Rolando does not run actually into the fissure of Sylvius, a convolution bridging across at that point; hence the lowest half inch or so of the line would cross this convolution. In those cases where the two fissures join, the fissure of Rolando would be indicated by the whole length of the line.

"*External Parieto-occipital Fissure.*—This fissure is more variable in its position than any of the other principal fissures of the cerebrum and conse-

A, Glabella   B, External occipital protuberance.   e a p, External angular process of frontal. BC, Transverse fissure   AB, Longitudinal fissure. Sy fis, Sylvian fissure.   Sy h fis, Horizontal limb of fissure of Sylvius   Sy a fis, Ascending limb of fissure of Sylvius   DE, Perpendicular line from depression in front of external auditory meatus to middle line of top of head   FG, Perpendicular line from posterior end of base of mastoid process to middle line of top of head   FH, Fissure of Rolando p o fis, Parieto-occipital fissure.   +, Most prominent part of parietal eminence.

quently any indication of it on the surface of the scalp must be only approximately accurate. If we continue the line for the horizontal limb of the fissure of Sylvius onwards to the line indicating the longitudinal fissure we shall find that on trephining over the inner inch of this line we shall expose the external parieto-occipital fissure, or some part of it. In most cases we have seen the whole of the fissure in the opening so made, in others it showed itself in the posterior half of the opening, and in still fewer cases it was seen in the anterior half."

Having thus indicated the principal fissures Professor Reid proceeded to map out the areas of the frontal, parietal, temporo-sphenoidal, and occipital lobes with their chief sulci and convolutions as far as they are in relation with the outer surface of the scalp. He says that his descriptions are taken from a series of dissections made by himself in the post-mortem room of St. Thomas's Hospital. They were frequently tested and had been found to be accurate. The observations were intended to give a general idea of the surface of the cerebrum in relation to the scalp.

THE   RADIOGRAPHY   OF   THE   DUODENAL   CAP

By G. R. MATHER CORDINER

ASSISTANT RADIOLOGIST, ST. GEORGE'S HOSPITAL

AND G. T. CALTHROP

RADIOLOGIST, PRINCESS BEATRICE HOSPITAL

IN the examination of the duodenum it can be claimed that modern radiography is more exact and more reliable than either clinical or laboratory investigation. In fact it will reveal more than all the other methods put together. Time and again it gives information which can be obtained in no other way at present available. It is the only means by which incontestable evidence of an ulcer can be obtained, including its exact situation, and whether single or multiple. It can go further. It will show the size and condition of the ulcer and the presence of complications, such as penetration or stricture, the result of scarring changes from healed ulceration, and sometimes even the likelihood of impending perforation. Thus the findings will help the clinician to estimate the relative value of medical or surgical treatment in any individual case.

It is the common experience that there are many pitfalls in the radiographic diagnosis of lesions of the cap. The X-ray findings frequently lack the decisiveness which might be expected from an examination which is essentially objective in character. This is due almost entirely to a failure to employ an appropriate technique in the examination of the cap. Diagnostic accuracy is inextricably bound up with technique. Provided an appropriate technique is employed, there is no portion of the alimentary tract which can be so thoroughly investigated and recorded as the duodenal cap. The radiological diagnosis of duodenal ulcer can then be made with almost mathematical accuracy, for in the majority of cases the inner aspect of the cap can be shown on the film as clearly as in the resected specimen. Such a technique is the 'aimed exposure with dosed compression' technique, evolved by Professor H. H. Berg, of Hamburg.

In the early days technical difficulties in radiography prevented a satisfactory representation of the cap. As a result diagnosis was based on indirect sign-complexes in which changes in the function and form of the stomach played a predominant part. The first real advance towards the demonstration of direct radiological signs in the cap was the result of the investigations of Cole,[1] and George and Gerber,[2] who advocated the serial radiography of the cap. By correlating clinical, radiographic, operative, and pathological findings it was established that an unchanging contour deformity of the duodenal cap, in the majority of cases, spoke for duodenal ulcer. Akerlund[3] was, however, responsible for the greatest advance in the demonstration of the direct ulcer sign. By applying varying degrees of pressure ('dosed compression') to the cap under screen control, the optimum degree of pressure for the isolation and demonstration of the ulcer niche was determined. Single or serial radiographs were then made. Berg[4] crowned and completed this work by the introduction of the 'aimed exposure'.

TECHNIQUE

The object of the Berg technique is to present the details of the mucosal surface of the cap. In order to carry out the examination, some modification of the conventional screening apparatus is necessary. Some means must be provided by which varying degrees of compression (dosed compression) can be applied to allow the presentation of the mucosal relief. In addition the screening stand and power unit must be so arranged that a film can be exposed at any moment during the course of screening. The delay between the observation of the image on the screen and the recording of it on the film must not exceed a fraction of a second. Thus an aimed exposure is made. These aimed exposures are taken at the most varied angles and positions whenever there is any suspicion of abnormality. They provide a permanent record which can be studied at leisure and will often show details which even the most experienced examiner cannot detect on the screen. The ordinary vertical screening stand can be adapted for this work, but it will be found that an appropriately designed tilting couch facilitates the examination, especially so in those cases which are difficult in the erect position.

THE MUCOUS MEMBRANE

The cap differs from the other parts of the duodenum and from the remainder of the small intestine in that it is devoid of valvulæ conniventes. Although it was generally regarded as free from folds, Forssell,[5] in his investigations on the alimentary mucous membrane, showed that the cap presents a more or less typical mucosal pattern. As a rule, the folds are arranged longitudinally, continuous with the folds of the pyloric canal. On the radiogram the folds are represented by the translucent spaces, whilst the intervening hollows are seen filled with opaque medium. The folds are not visible when the cap is filled, but come into view when the superfluous opaque medium is displaced by pressure.

The mucosal folds are not permanent anatomical structures, but vary during the process of digestion, so that a transverse arrangement of the folds, or a complicated rhomboidal, 'criss-crossed', or honeycomb pattern may be obtained. Thus a cap may

FIG. 472.—Normal mucosal relief pattern of duodenal cap. X, Pylorus.

show a varying mucosal pattern during the course of an examination. *Fig.* 472 shows a typical example of normal mucosal relief pattern.

The normal mucosal folds are soft and elastic and can be deformed and obliterated by stretching or by pressing over the cap. When a mild degree of pressure is applied, a broadening of the folds at first takes place and is associated with a corresponding narrowing of the intervening hollows. By increasing the amount of pressure the mucosal pattern can be completely obliterated. When, however, duodenitis or ulcer and its associated scarring changes pathologically

alters the mucous membrane, the mucosal folds are less easily influenced by pressure. Thus it is that pressure sufficient to obliterate normal mucosal folds brings into relief the details of the pathologically altered mucous membrane. The demonstration of a normal mucosal pattern in the cap definitely excludes the presence of an ulcer.

DUODENITIS

Amongst others, Judd and Nagel,[6] and Konjetzny[7] have shown that a chronic inflammation of the duodenal mucous membrane may occur even when no ulcer is present. This condition of duodenitis presents a clinical picture so similar to that of chronic duodenal ulcer that their clinical differentiation is seldom possible.

At operation the duodenum may appear normal, both to inspection and palpation. Often in the milder forms the only visible evidence on the serous surface of the duodenum is a localized area of hyperæmia with stippling, though the latter may only come into view when the serous surface is rubbed. In more advanced cases these signs are more marked and there may be a uniform narrowing of the duodenum for a distance of a few centimetres. There is, however, no evidence of scarring such as is found with ulcer. On palpation the wall of the duodenum seems normal and there is no induration such as is found with ulceration. When the duodenum is opened the mucous membrane is seen to be reddened and œdematous and may show minute superficial erosions. The lesions may be either localized or diffuse. As a rule the inflammatory process is limited to the mucosa. In some instances the submucosa shares in the inflammatory reaction, and the condition may be found, of course, in association with a chronic ulcer.

MacCarty[8] describes the pathological picture of duodenitis as that of cellular destruction with congestion, œdema, and migration of polymorphonuclear leucocytes, lymphocytes, and endothelial leucocytes.

The exact relationship between duodenitis and duodenal ulcer is not clear. Judd holds that duodenitis is not a stage from which true ulceration invariably develops, since the average duration of the symptoms of the two lesions is about the same. On the other hand, Konjetzny has found all stages from simple cellular infiltration of the mucosa and superficial erosions to large chronic, calloused ulcers in the same specimen. According to Kirklin,[9] the fundamental radiological characteristic of duodenitis is an extreme degree of irritability of a cap which is grossly deformed and contracted. Characteristic of such a deformed cap is its feathery and indistinct contour. The deformity, in addition to being much more extreme than with ulcer, is a changing one. Occasionally the cap may momentarily fill out and show a normal contour. The mucosal pattern is coarsely and irregularly reticular and is depicted as translucent islets lying in a dense network.

Berg has pointed out that direct changes can be demonstrated in the mucosal relief of the cap in cases of duodenitis. These changes are analogous with those which are found in the gastric mucosal picture in cases of hypertrophic gastritis. The latter condition is frequently to be found in association with duodenitis, and, though most commonly limited to the pyloric portion of the stomach, is sometimes generalized.

The most constant feature of a duodenitis is a veiling of the mucosal pattern by inflammatory exudate and a broadening and stiffening of the mucosal folds.

Not only are the folds broadened but so are the intervening hollows (*Fig. 473*). Duodenitis must not be diagnosed because of broadening of the mucosal folds unless they show changes in consistence. As the folds are examined under the screen they appear to have lost their elasticity, and give the impression that they have been starched. They can no longer be obliterated by stretching the duodenum and they are less easily deformed by pressure. Although the normal mucosal pattern may be retained, yet the folds often show abnormal direction (*Fig. 474*). Frequently deposits of the opaque medium may be retained between the swollen and abnormally directed folds and such deposits may simulate and be difficult to differentiate from a true niche. As a rule these pseudo-niches are larger and more irregular than a true ulcer niche, and do not fulfil the radiological criteria of niche formation when examined in both *en face* and profile views. Further, it is characteristic of such deposits that they are inconstant in situation during the same and also at subsequent examinations. These changes are most commonly seen in the
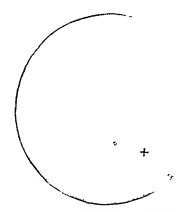
FIG. 473.—Duodenitis. Aimed exposure with dosed compression showing stiffened and broadened mucosal folds. X, Pylorus.

FIG. 474.—Duodenitis. Showing swollen mucosal folds with irregular pattern. X Pylorus.

cap, but similar changes may be present in the descending portion of the duodenum. Berg, however, points out that it is uncommon to find them beyond the papilla of Vater—in other words, they are localized to the common ulcer sites.

Dense adhesions and periduodenal tumour-mass formations such as occur with penetrated ulcers are not found in duodenitis. Nevertheless, as the result of fine connective-tissue deposit on the serous surface of the duodenum, fine filamentous adhesions to the omentum, gall-bladder, and other organs may form. Such adhesions may produce no deformity of the contour, nor diminish the mobility of the duodenum, and consequently may escape radiographic recognition. When, however, adhesion takes place between the gall-bladder and the duodenum a characteristic deformity is often produced. Normally in the oblique positions, the junction of the cap and the descending portion of the duodenum is seen as a nicely rounded curve. When adhesion occurs between the gall-bladder and duodenum, this rounded curve is replaced by a persistent, acute angulation (*Fig. 475*A, B). In these cases cholecystographic examination will often show that the gall-bladder is drawn towards the mid-line, but its contour is normal, a good concentration of

the dye is obtained, and there is a normal contractile response to a fatty meal. Occasionally an adhesion will produce a small boss of the duodenal contour in the profile view and so simulate a niche (*Fig.* 475C). The differentiation can be made
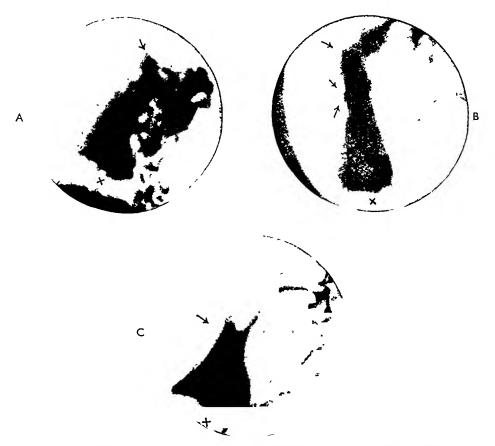
FIG. 475.—Acute angulation at junction of cap and descending limb of duodenum, the result of adhesion to the gall-bladder. A, Confirmed at operation. B, Upper arrow indicates site of adhesion. Lower arrows point to ulcer niche on anterior wall. At operation adhesion confirmed. Scar on anterior wall of cap. C, Duodenal boss due to adhesion. Note absence of concave indentation of adjacent profile. X, Pylorus.

because the concave indentation of the profile on either side of the boss is lacking. This concave indentation, as has been stressed by Berg, is an essential accompaniment of a true niche.

THE NICHE

The niche is pathognomonic of an ulcer in the duodenum as in the stomach. It is the only absolute evidence of loss of substance from ulceration, and with proper technique it is the most constant demonstrable sign. Whilst some recent publications emphasize the rarity of the direct sign—the niche—in the duodenum, others do not even mention it. The failure to realize the frequency and importance of the niche can only be due to failure in radiographic technique.

The conditions for the demonstration of the niche are particularly favourable, since, with few exceptions, ulceration in the duodenum is confined to the cap. The area to be examined is relatively small, and in the majority of cases every aspect of it can be thoroughly investigated and recorded. Whenever possible, the presence of a niche should be confirmed in two planes. Usually this can be done. Sometimes, however, it may be difficult and in a few cases impossible—for example, when there are extensive adhesions or in adipose individuals with a high-lying steer-horn stomach.

A niche has essentially two components : the crater filled with opaque medium, and the defects produced in the duodenal lumen by the reactive tissue changes in the immediate vicinity of the ulcer. Berg has laid down certain criteria to which a niche must conform. These criteria are absolute, since they can be interpreted and confirmed in terms of the pathological changes which occur with ulceration.

The *en face* niche—that is, the niche as viewed from its front—is seen most often when the patient is examined in the first or right anterior oblique position. The niche is usually hidden or is indistinct when the cap is distended, but can be isolated and recognized by applying a suitable degree of compression (*Figs.* 476, 477). Such niches as are seen only after compression are termed by Berg ' relief ' niches. In the ulcer of comparatively short duration the niche is represented by a dense, circular or oval, well-defined opaque deposit surrounded by a translucent halo, or, as Berg calls it, a ' ring wall ' (*Figs.* 476B, 477B). This ring wall is produced by the œdematous mucous membrane surrounding the ulcer and projecting into the duodenal lumen. In the more chronic ulcer the niche is usually smaller, and the ring wall cannot generally be seen in this view. Distinct folds of mucous membrane will, however, be seen converging in a star-like manner towards the crater (*Fig.* 478). This convergence of the mucosal folds is the result of the fibrosis and reactive contraction which accompanies the chronic ulcer.

Since in the majority of cases ulceration in the cap is found on the antero-lateral and postero-medial surfaces, the profile niche is best shown by examining the patient in the second or left anterior oblique position. The characteristic—indeed, the essential—feature of the profile niche is a projection from the contour with a concave indentation of the adjacent profile on either side (*Fig.* 479). In the recent ulcer this concave indentation is produced by the swollen mucous membrane surrounding the ulcer and corresponds to the ring wall of the *en face* view when seen at right angles (*Fig.* 480). In the chronic ulcer it is produced partly by swollen mucous membrane, partly by infiltrative thickening of the wall surrounding the ulcer, and partly as the result of scar-tissue contraction in the wall.

It is important to recognize when an ulcer has penetrated into a neighbouring organ. If one judges by the usual clinical standards—disappearance of symptoms for months or even years, and the absence of occult blood from the stools—penetrated ulcers may show an apparent cure by medical means. It can be shown radiographically, however, that such ulcers are invariably quite refractory to medical treatment.

Normally the duodenal cap can be freely moved on manipulation. When an ulcer has penetrated into a neighbouring organ the cap becomes fixed at this point, and such fixation can be determined by palpation during the screen examination. If the pancreas has been penetrated the posterior wall of the duodenum becomes
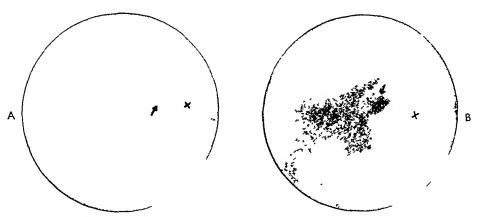
FIG. 476.—A, Aimed exposure.   Faint shadow of niche.   B, Aimed exposure with dosed compression.   Niche with ring wall, due to swollen mucous membrane.   X, Pylorus.
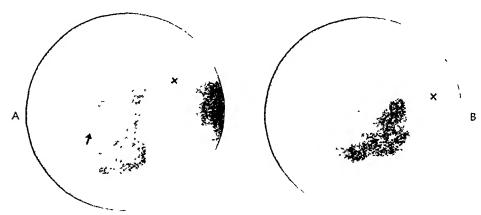
FIG. 477.—A, Aimed exposure.   Niche with ring wall.   B, Aimed exposure with dosed compression.
Same case.   X, Pylorus.
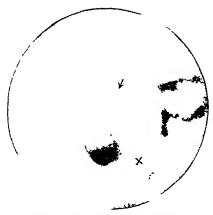
FIG. 478.—*En face* niche with star-like convergence of mucosal folds.   X, Pylorus.
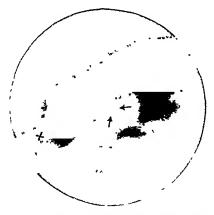
FIG. 479. — Profile niche, posterior wall. Concave indentation of adjacent profile.   X, Pylorus.
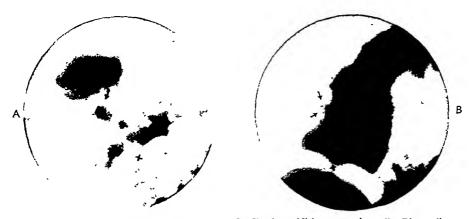
FIG. 480.—A, *En face* niche with ring wall.   B, Profile view.   Niche on anterior wall.   Ring wall of *en face* niche shows as concave indentation of profile on either side of ulcer.   X, Pylorus.
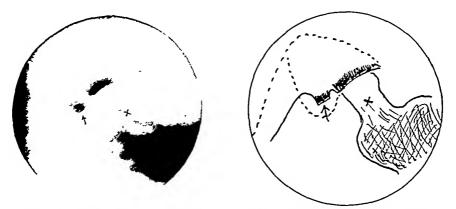
FIG. 481.—Posterior wall ulcer penetrated into pancreas.   V-shaped deformity with niche. X, Pylorus.   (Confirmed at operation.)
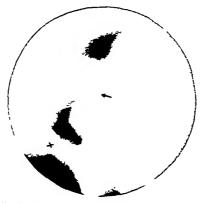
FIG. 482.—Posterior wall ulcer penetrated into pancreas.   V-shaped deformity with niche. X, Pylorus.   (Confirmed at operation.)

V-shaped when 'put on the stretch', and an ulcer niche will be found at the junction of the limbs of the V (*Figs.* 481, 482).   Sometimes an accessory pocket with a communicating channel is seen outside the duodenal lumen (*Fig.* 483A).   Occasionally one can show mucosal folds bent sharply away from the normal longitudinal direction and pointing into the channel (*Fig.* 483A). In the usual postero-anterior view the cap is seen foreshortened on account of its peculiar lie.   Normally when the patient is placed in the right or left
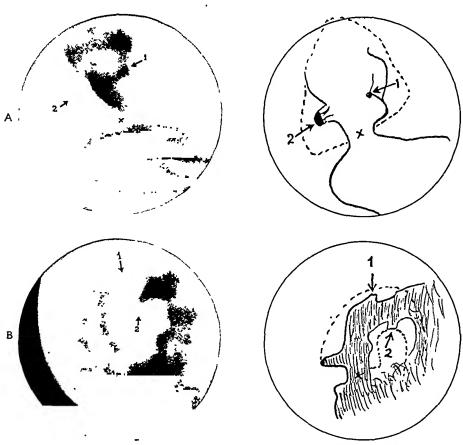
FIG. 483.—Posterior wall ulcer penetrated into pancreas.   A, *En face* view.   2, Penetrated ulcer on posterior wall, showing accessory pocket and divergence of mucosal folds.   1, Anterior wall ulcer. B, *Profile view of niches.   V-shaped deformity of posterior wall with niche.   Cap foreshortened* in this view on account of fixation.   X, Pylorus.   (Confirmed at operation.)

anterior oblique positions the foreshortening disappears.   If, however, the duodenum is fixed as the result of the penetration of an ulcer, the foreshortening persists in all positions.

The characteristics of a penetrating ulcer[10] may be summarized : (1) Fixation of cap; (2) V-shaped deformity with niche; (3) Accessory pocket; (4) Divergence of mucosal folds into communicating channel; and (5) Foreshortening. Although these characteristics may not be seen in every case, yet, if several are present, penetration may be deduced.

Multiple ulcers are common. Usually they are the 'kissing' ulcers of Moynihan. In the *en face* view the niches may be superimposed (*Fig.* 484A), but by turning the patient slightly, the two niches can be isolated (*Fig.* 484B).

FIG 484 —'Kissing' ulcers   A, *En face* view—niches superimposed   B, *En face* view—niches isolated by turning patient slightly.   C, Profile view of niches   X, Pylorus   (Confirmed at operation)
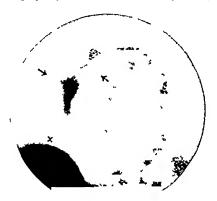
FIG. 485 —Two ulcers in cap.   Profile view.   1, Recent ulcer on anterior wall.   2, Chronic ulcer in distal portion of cap on posterior wall.   X, Pylorus.

Confirmation of the niches is, of course, obtained in the profile view (*Fig.* 484C). The niches may be situated at different levels (*Fig.* 485), and three or more niches may be isolated in a cap (*Fig.* 486).
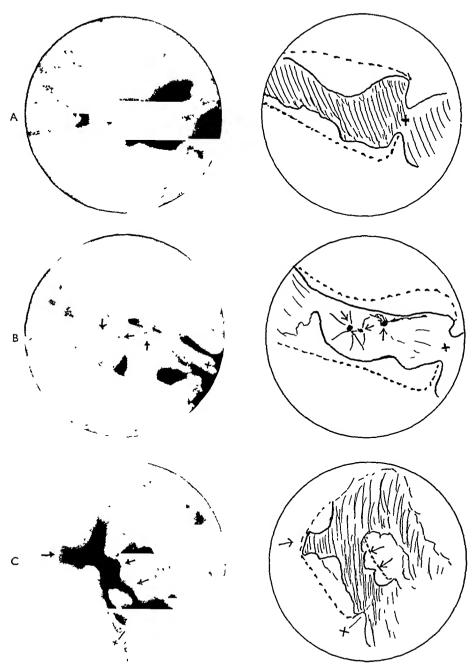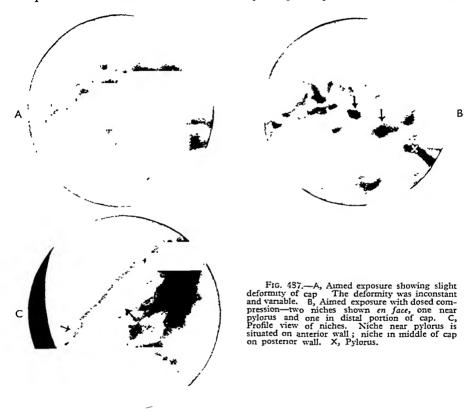
FIG 486.—A, Aimed exposure showing deformed cap.   B, Aimed exposure with dosed compression showing three niches *en face*.   C, Profile view of niches.   X, Pylorus.

Despite advances in technique, it must not be thought that every duodenal ulcer can be detected by X rays. Obviously, small shallow ulcers which do not retain the opaque medium will defy radiographic recognition. Under certain conditions even relatively large ulcers may be difficult to show. Berg holds that after a recent hæmorrhage a crater may be filled with blood-clot. The crater may also be blocked by mucus or by food remnants. In such a case the niche will be seen by giving a second meal immediately after the first has left the stomach and has exerted a cleansing effect upon the mucous membrane. Forssell holds that the 'autoplastik' of the mucous membrane may temporarily seal off the ulcer crater

FIG. 487.—A, Aimed exposure showing slight deformity of cap The deformity was inconstant and variable. B, Aimed exposure with dosed compression—two niches shown *en face*, one near pylorus and one in distal portion of cap. C, Profile view of niches. Niche near pylorus is situated on anterior wall; niche in middle of cap on posterior wall. X, Pylorus.

from the duodenal lumen. Thorough palpation must always be employed so as to force the opaque medium into the crater.

A criticism which is often directed against the compression techniques of both Berg and Akerlund is that, by compression, deposits can be isolated and will be mistaken for ulcer-niches when, in fact, no ulcer exists. This will only occur if the fundamentals of technique and interpretation are not completely mastered. Provided a niche is only diagnosed when the strict criteria laid down by Berg are satisfied, the danger of diagnosing a non-existent ulcer is negligible. This has been proved beyond all doubt by the careful operative control of the radiographic findings.
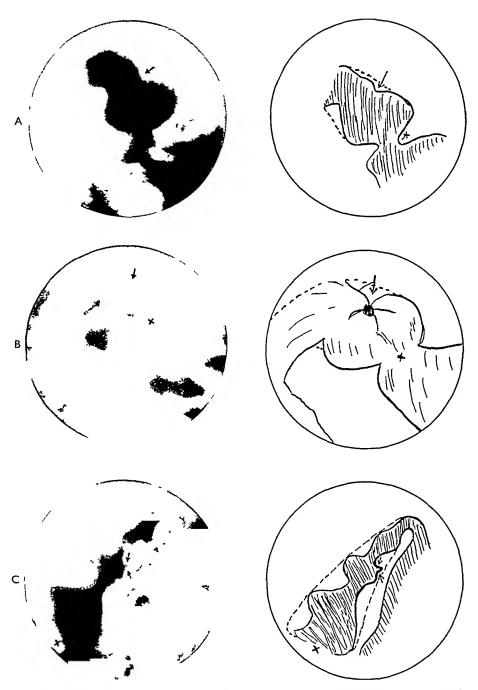
FIG 488 —A, Aimed exposure   Circular narrowing of cap which is otherwise normal   B, Aimed
exposure with dosed compression, showing *en face* niche with converging mucosal folds at site of narrowing
C, Niche shown in profile on posterior wall   Gross deformity of cap in this view is due to inflammatory
swelling of the mucous membrane, the result of duodenitis   X, Pylorus
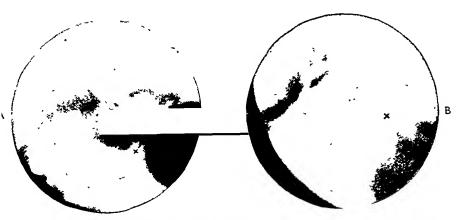
FIG. 489.—A, Aimed exposure showing typical deformity of duodenal cap. B, Aimed exposure with dosed compression. Scarring changes of healed ulceration. No ulcer niche present. X, Pylorus.

FIG. 490.—A, Aimed exposure showing deformed cap. Cicatricial deformity of greater curvature. Inflammatory deformity of lesser curvature close to pylorus. B, Aimed exposure with dosed compression. *En face* view. Niche on anterior wall. Scarring changes on posterior wall with stiffened folds. C, Profile view. Niche localized on anterior wall. Posterior wall shortened, with loss of normal convexity, the result of scar-contraction of healed ulceration. X, Pylorus.
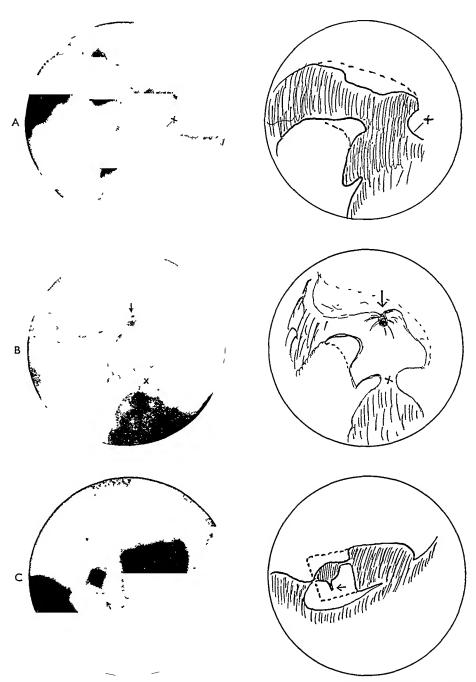
FIG. 491.—A, Aimed exposure. Typical deformed duodenal cap. B, Aimed exposure with dosed compression. *En face* niche in mass of scar tissue. C, Profile view. Niche on posterior wall. X, Pylorus. (Confirmed at operation.)

The deformities of the duodenal cap—the trefoil, the coral-like, the pine-tree, to mention but a few—are of importance. Yet a deformity of the cap, as the term is generally understood, is not the cardinal sign of ulcer, and should not be so used. Firstly, in more than 50 per cent of cases of duodenal ulcer the classical deformities are not present (*Figs.* 487, 488). Secondly, whilst it is true that a contour deformity of the cap may, and frequently does, signify the presence of an ulcer, this is not necessarily the case. As an ulcer involving the deeper layers of the duodenum heals, fibrosis and scarring occur. It is to this in the main that the classical deformities are due. It is natural, therefore, that deformities can be shown in patients whose ulcers have healed and who are free from symptoms (*Fig.* 489). Deformities of the cap are due or are ascribed to many conditions : duodenal ulcer, healed ulcer, duodenitis, cholecystitis, appendicitis, incomplete or fleeting filling, and periduodenal adhesions. The possibilities of misinterpretation are obvious and make deformity of the cap too unreliable a sign on which to base the diagnosis of duodenal ulcer. Moreover, if an ulcer is present, it is possible even in the most grossly deformed cap to isolate and demonstrate the ulcer niche (*Figs.* 490, 491). The importance of a deformity lies, not in its value as a sign diagnostic of ulcer, but as evidence of alteration in the lumen of the cap and thus a potential or active cause of gastric dysfunction.

The radiological picture corresponds to a plastic impression of the mucosal surface of the duodenal cap. The conditions prevailing there at the time of the radiological examination do not necessarily show on the serous side. This applies particularly to ulcers which are comparatively superficial, and have not penetrated to any extent into the deeper layers of the duodenal wall. Sometimes, therefore, after the radiological demonstration of an ulcer niche in the cap, the surgeon at operation is unable to detect evidence of ulceration. This is also true of some chronic ulcers, especially if they are situated on the posterior wall and at some distance from the pylorus where they are difficult of access. Further, if an interval has elapsed between the barium meal examination and the operation, the ulcer may have healed as the result of medical treatment. Before the radiological diagnosis is refuted, the duodenum must be opened and the inner aspect of the cap examined. Also every case in which a period of time has intervened should be re-examined a day or two before operation.

With the isolation and recognition of the ulcer niche the nature of the lesion is clear. No other radiological evidence is necessary for diagnosis. If no ulcer niche can be isolated, the statement that an ulcer is present in the duodenum at the time of examination is radiologically unjustified.

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ENCRUSTATION OF THE BLADDER AS A RESULT OF ALKALINE CYSTITIS

By H. G. LETCHER and N. M. MATHESON

CENTRAL MIDDLESEX COUNTY HOSPITAL, LONDON

ALTHOUGH calcareous deposits of a somewhat localized extent are not infrequently observed in the more chronic types of urinary disease, generalized encrustation of the bladder wall is far from common. The following case, occurring in a young patient, illustrates several characteristic features of the advanced condition.

CASE REPORT

M. P., a woman of 26 years who was the mother of one child and again in the early months of pregnancy, entered hospital on Jan. 29, 1935. Slight urinary frequency following a confinement three years previously was not attended by serious inconvenience. The onset of lower abdominal discomfort accompanied by extremely frequent and painful micturition—each of four days' duration—caused the patient to seek advice.

Systemic investigation disclosed no unusual findings, except that the offensive alkaline urine contained albumin, phosphates, and pus—a profuse growth of B. coli being subsequently obtained on culture. Radiological examination showed a clearly defined bladder outline (*Fig.* 492). A capacity of only 4 oz. and troublesome hæmorrhage rendered cystoscopy difficult, but after prolonged irrigation good views were secured. The irregularly contracted bladder walls were heavily coated with whitish encrustations (*Fig.* 493), bleeding necrotic areas being visible when fragments were detached. Besides the extensive surface deposits, stalactitiform masses were freely suspended, and sharply defined plaques occupied the vault (*Figs.* 494, 495). The ureteric orifices tended towards the golf-hole type, and specimens from each renal pelvis were acid although the bladder urine was strongly alkaline.

Numerous attempts were unsuccessful to isolate the B. proteus ammoniæ from the urine, and relevant tests failed to give any evidence of genito-urinary tuberculosis.

After twelve days' treatment with acid bladder irrigations (acid acetic B.P. 2 drachms to a pint of water) twice daily, cystoscopy showed a remarkable change. The interior was now free from all phosphatic concretions, but well-defined areas of ulceration were present in the mucosa (*Fig.* 496). Mercuric oxycyanide (1–4000) was substituted for the local acetic acid treatment. On viewing the bladder after ten days, recurrence was obvious on the anterior wall, the deposits now taking the form of smaller plaques surrounding the shallow ulcers. After re-instituting the acid lavage for another six days, further improvement ensued; the ulcers were smaller, of the healing type (*Fig.* 497), and only two small encrustations remained. Acid irrigations were continued for another six weeks.

When examined on May 10, 1935, after a fortnight without local treatment, the patient was free from urinary symptoms. The bladder capacity was 10 oz. and thin stellate scars occupied the sites of the former ulcers. No concretions were present, the left ureteric orifice was of normal appearance, and the right only slightly dilated. The patient was discharged on May 22.

After a normal confinement at the end of August, she returned for further observation (as requested) on Oct. 19. Cystoscopy revealed only the scarring of the previous ulceration without any trace of phosphatic deposits, although no treatment had been given since discharge.

DISCUSSION

Encrusted cystitis as defined by François[1] is a more or less localized ulcerative inflammation of the bladder wall with deposits of phosphate of lime on the surface and in the walls of the ulcerations.

After prolonged studies, Hager and Magath[2] came to the conclusion that encrusted cystitis with alkaline urine is caused by the implantation of *B. proteus ammoniæ* in a bladder which is already the seat of some form of inflammatory or
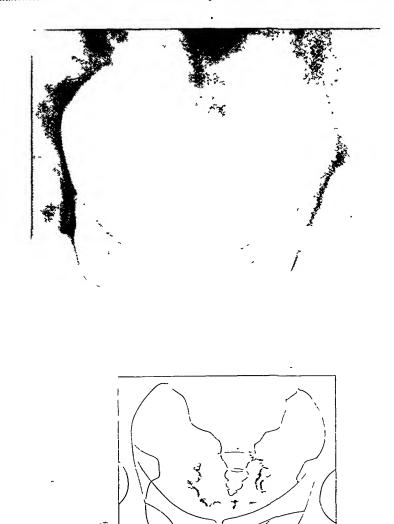
FIG. 492.—Skiagram showing crenated outline of encrusted vesical walls.

tumorous lesion. The encrustations result from the breaking up of urea into carbon dioxide and ammonia with the precipitation of alkaline inorganic salts.

The earlier writers on this subject observed the condition almost exclusively in women. A more recent review by Hager[3] of fifty cases at the Mayo Clinic shows the disease to be over twice as common in females as in males. He states that the condition prevails in married women and during the child-bearing period,
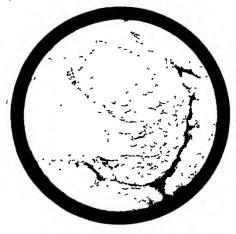
FIG 493.—Cystoscopic view of encrustations. Bladder wall irregularly contracted as seen in skiagram. Mid-field simulates appearances of calculus. Soft downy deposits are seen projecting from the right.
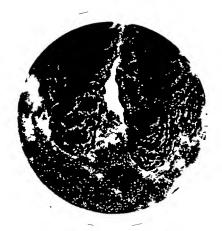
FIG. 494.—Elevated or tumour-like encrustations of the stalactite type.

FIG 495.—Flat or surface deposits, with sharply defined irregular edges, on the inflamed bladder wall.
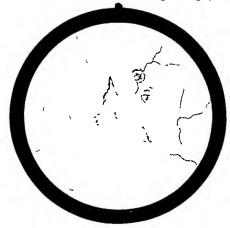
FIG. 496.—Ulcer as observed twelve days after treatment began.

FIG. 497.—Healing ulcer—one month after treatment began.

the presumption being that trauma of the bladder and catheterization are contributing factors. In males, however, the disease appears more usually during the prostatic age.

The symptoms are those of severe chronic cystitis of variable duration—often preceded by attacks of a milder nature. Hæmaturia is repeatedly mentioned as a salient feature, and the passage of calculous material has been sometimes noted. The urine is generally alkaline, cloudy, and foul-smelling; it contains mucus, blood, and a varying quantity of pus. Specimens collected from the kidneys, however, are sometimes distinctly acid even when the bladder urine is alkaline—a fact frequently commented upon in urological literature.

Cystoscopy renders the diagnosis certain, but is often difficult, complicating factors being the high degree of vesical irritability and the tendency to profuse hæmorrhage. Some cystoscopical appearances may now be briefly mentioned.

1. *Cystitis* is as a rule very marked, particularly in the neighbourhood of the encrustations; œdema, which may obscure the ureteric orifices and even involve the urethra, is said to be a feature.

2. *Calcareous deposits* characterize the disease: these are firmly connected with the bladder wall and are of widespread or local distribution. According to the writings of Caulk[4] two varieties are encountered either alone or in association.

a. The flat or surface type—more commonly seen behind strictures, prostatic obstruction, around vesico-vaginal fistulæ, and capping bladder tumours.

b. The elevated or tumour-like type—this is the rarer and is due to constant precipitation of salts on an already encrusted ulcer.

3. *Ulceration*, which appears to be the essential lesion, occurs in any area of the bladder. Multiple lesions of varying size are commonly found, the condition in reality being one of chronic ulcerative cystitis. The irregular ulcers serve as nidi for precipitation of salts and usually involve the mucosa, but occasionally penetrate more deeply.

François was of the opinion that encrusted cystitis never disappeared spontaneously and did not readily yield to medical treatment.

Rendering the urine acid by the administration of such drugs as sodium acid phosphate and ammonium chloride is of little avail in ameliorating this infection. The beneficial effects of bladder lavage with acid solutions are usually very transient, the rapid disappearance of the concretions being followed, in the great majority of instances, by an equally rapid re-formation. More favourable results are expected from prolonged acidification by ketogenic diets or their more recent chemical substitutes. Caulk is an advocate of the intravesical injection of Bulgarian bacilli, the idea of such treatment being to have the organisms proliferate and produce an acidity which would be incompatible with the life of the organisms responsible for the disease.

Numerous surgical methods have been employed to eradicate the diseased mucous membrane, which forms the basis for the calcareous formations. Hager favoured intensive local treatment. Writing in 1926, he stated that experience has taught that the most consistently satisfactory results were obtained by the removal of all encrustations by means of curettement and topical applications of strong silver nitrate solution to the denuded areas.

In view of the well-known experiments on vitamin deficiency factors in urolithiasis and of the researches of Hunter[5] and others on calcium metabolism

attempts have been made to treat this form of cystitis on more general lines Redewill[6] quotes an instructive recurrent case. By intensive vitamin therapy and the administration of parathyroid the tendency to recurrence was completely checked.

SUMMARY

Some noteworthy features of the present case may be recapitulated :—

1. The onset of the attack in the early months of pregnancy.

2. Almost the entire bladder was affected.

3. The bladder wall was outlined in skiagrams.

4. Although the voided urine was strongly alkaline, specimens secured by ureteric catheterization were acid.

5. Repeated examinations failed to isolate the *B. proteus ammoniæ* from the urine.

6. The remarkable benefit which followed lavage with acid solutions appears to be unusual.

We wish to express our thanks to Mr. Thornton Shiells for his illustrations of this article.

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SPONTANEOUS RUPTURE OF EXTENSOR POLLICIS LONGUS TENDON ASSOCIATED WITH COLLES'S FRACTURE

By THOMAS MOORE

JUNIOR SURGICAL REGISTRAR, ROYAL VICTORIA INFIRMARY, NEWCASTLE-UPON-TYNE

THE object of this paper is to report three cases of spontaneous rupture of the extensor pollicis longus tendon associated with Colles's fracture.

CASE REPORTS

Case I.—Miss R., aged 25 years, fell on her left wrist on Dec. 19, 1933. When seen the next day she was found to have a Colles's fracture with dorsal rotation of the lower fragment but no radial displacement. The fracture was reduced under local anæsthesia,

FIG. 498.—*Case* 1. The patient is unable to extend the interphalangeal joint of the thumb.
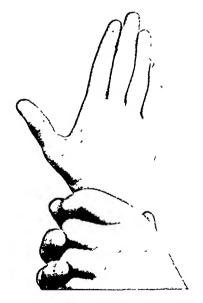
FIG. 499.—*Case* 1. Showing the result obtained by tendon transplantation.

a non-padded plaster cast applied, and active movements of the fingers and thumb encouraged from the beginning. Plaster was removed on Jan. 10, 1934. The fracture was healed in good position. The patient had 50 per cent of normal range of movement in the wrist and inferior radio-ulnar joints. Finger and thumb movements were practically normal. Physiotherapy (aerated baths and active movements) was started. On Jan. 21, 1934, the patient discovered that she could not extend the terminal joint of the thumb (*Fig.* 498).

Examination showed healed Colles's fracture with full function of all joints but inability to extend the interphalangeal joint of the thumb. She was unable to make the medial boundary of the anatomical snuff-box prominent. No movements of the interphalangeal joint of the thumb could be obtained by electrical stimulation of the extensor pollicis longus muscle. On Feb. 6 Mr. Gordon Irwin explored the tendon through a vertical incision 5 in. long across the dorsal aspect of the wrist. The tendons crossing the lower end of the radius were exposed, but that of the extensor pollicis longus was missing from its groove on the medial side of Lister's tubercle. Its place was taken by some yellowish soft tissue. The distal end of the tendon was found just below the lower edge of the dorsal carpal ligament. It was flattened, soft, and frayed. The proximal end was bound down to the bone just above the site of fracture and was much attenuated. End-to-end suture was not possible. The distal end was pulled through the tendon of the abductor pollicis longus and sutured to it with fine catgut sutures, the thumb being held in full abduction and extension. The wound was closed. The hand was put in splints which held the wrist in full dorsiflexion and the thumb in full extension and abduction. The splint and sutures were removed after three weeks, and physiotherapy started (aerated baths and movements). The patient was discharged on March 6 with a functionally normal hand (*Fig.* 499).

Case 2.—Mrs. B., aged 58 years, fell on her right arm on Dec. 11, 1933, and was seen in the fracture clinic the next day, when she was found to have a right Colles's fracture with no displacement. A non-padded plaster cast was applied and immediate active movements encouraged. The plaster was removed on Jan. 3, 1934. On Jan. 31 the patient complained of being unable to extend the interphalangeal joint of the thumb, and was found to have all the signs of rupture of the extensor pollicis longus tendon. The tendon was explored on Feb. 6 by Mr. Gordon Irwin. It was found in a condition similar to that of *Case* 1. The distal end of the tendon was transplanted into that of the abductor pollicis longus. The patient was discharged on June 4 with a functionally normal hand.

Case 3.—Mr. H., aged 57 years, slipped in the street on March 15, 1934, and was seen in the fracture clinic the same day, when he was found to have a right Colles's fracture with dorsal displacement and rotation of the lower fragment but very little radial displacement. It was reduced under nitrous oxide anæsthesia and a non-padded plaster cast was applied. The plaster was removed on April 5. On April 15 the patient noticed that he could not straighten the end of his thumb. Examination showed that he was suffering from rupture of the extensor pollicis longus tendon. I explored this on April 27, when the usual picture of spontaneous rupture of the tendon was found. The distal end was transplanted into the tendons of the abductor pollicis longus and the extensor pollicis brevis. The patient made a good recovery, except for a temporary slight median nerve paralysis due to the tourniquet which was used during the operation. He returned to work on July 9 with a functionally normal hand and reports he has been doing full work since.

DISCUSSION

Normal tendons are so strong that their rupture is rare. When great strain is placed upon them they usually tear away from their periosteal attachment, often with a flake of bone, as is commonly seen in the extensor tendons of the fingers, or solution occurs at the musculo-tendinous junction. Adams has reported a very interesting case of the latter type. A seaman jammed his hand in a doorway. Drawing the hand away he sustained a traumatic amputation of the distal phalanx of the middle finger, attached to which were 15 in. of the tendon of the flexor digitorum profundus which had torn away at the musculo-tendinous junction.

When a tendon is weakened by disease, rupture may occur during ordinary use, constituting the so-called ' spontaneous ' rupture; ' pathological ' rupture would be a better term. In cases of definite infective tenosynovitis such a result might be expected. Mason collected ten cases from Kanavel's records of tuberculous tenosynovitis.

Much more fascinating are those cases in which pathological tendon rupture is a consequence of trauma. The extensor pollicis longus tendon is classically the one affected. The condition was first described as affecting the hands of drummers in the German Army, giving rise to ' drummer's palsy '. The tendon, the seat of a chronic aseptic inflammation due to the repeated trauma sustained in the use of the left drum-stick, undergoes gradual solution. Later cases of rupture of this tendon were reported following injuries about the wrist, usually but not always associated with a fracture of the radius. In 1932 McMaster reported a case and could find only twenty-seven recorded cases in the literature dealing with the condition.

The etiology of the affection has been much disputed. It has been pointed out that the tendon with the wrist dorsiflexed makes two distinct angular bends— one round Lister's tubercle, and the other round the lower end of the dorsal carpal ligament. Any weakening of the tendon would lead to its giving way at one of these sites. Various writers have noted that the tendon in its osseo-fibrous tunnel has a very limited mesotendon. Weigeldt has shown that the vascular supply decreases after twenty-five years of age. Practically all reported cases have occurred after this age. Axhausen thought that the irregularity of its bony groove following the healing of a fracture might lead to the gradual fraying and solution of the tendon. Others believe that the damage occurs at the time of fracture, possibly caused by a sharp fragment of bone. Kleinschmidt produced a typical radius fracture in cadavers and showed that the tendon of the extensor pollicis longus was lacerated by a loose fragment of bone in every case. In Ashhurst's case the tendon had become adherent in the callus and this had apparently led to the rupture. In most of the recorded cases the condition had been attributed to tendon damage at the time of injury or mesotendon damage with consequent disturbance of the vascular supply.

The rupture usually occurs between seven days and seven years after the injury (Honigmann), although three weeks to three months is the average period. The rupture occurs without any pain or excessive use, but in one case it was preceded by a violent muscle cramp.

The three cases here reported occurred in the first five hundred patients treated in the Orthopædic Department of the Royal Victoria Infirmary, Newcastle-upon-Tyne, by the non-padded plaster cast with immediate active movements as advised by Böhler. When patients so treated are encouraged to move the part, it is often noted that finger movements are free and painless, while movement of the thumb occasions pain. As no case has been recorded in the hospital out of many hundreds treated previously with immobilization for seven to ten days followed by massage and movement a possible etiological factor is suggested. In a Colles's fracture the tendon of the extensor pollicis longus owing to its anatomical position must be contused. Active use might thus lead to its gradual solution at one of the sites of angulation. In one of the cases there was no displacement of the bony fragments so that no damage could have been inflicted upon the tendon by them. In another there was some comminution of the lower fragment, and a sharp spicule of bone is visible on the X-ray films, so that primary laceration of the tendon described by Kleinschmidt might have occurred. The intervals between the occurrence of the fracture and the spontaneous tendon rupture were 31, 33, and 51 days. At operation in each case the tendon ends were swollen, softened,

My thanks are due to Mr. C. Gordon Irwin, under whose care the patients were, for permission to publish these cases and for his helpful advice and stimulating interest.

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SOLITARY PLASMOCYTOMA OF LONG BONES

By JUDSON T. CHESTERMAN

SURGICAL REGISTRAR, SHEFFIELD ROYAL HOSPITAL

THIS condition, which shows considerable similarity to endosteal sarcoma, is of interest partly on account of its rarity but mainly because of the better prognosis it offers to life and limb than the far more common osteogenic growths.

Both the origin of the cells and the pathogenesis of the tumours are very debatable points. There are two main theories with regard to the histogenesis of the cells : (1) That they are derived from blood-forming elements ; and (2) That they arise from the adventitial cells of the small blood-vessels. No final opinion can be given, but clinically the evidence is suggestive of the latter origin, for if the first were true, one would expect plasma cells to be a not uncommon occurrence in the blood instead of a rarity ; also, though several cases of pseudo-leukæmia[12, 13] with associated involvement of lymphoid tissue are recorded, only one case of plasma-celled leukæmia has been reported.[14] Opinions are again divided on the equally vexed question whether the tumours are neoplastic or granulomatous in nature. The consensus of opinion of those who have studied the bone cases is that the condition is a true neoplasm, for, as Stewart points out, the plasma cell is the only cell present, it is very variable in size but tends to be larger than that found in any known granuloma, and mitotic figures are frequent.[8] Ewing agrees with this view,[15] but Kaufmann and others whose chief experience is with the extra-osseous lesions consider it may be a granuloma.[16]

Plasma-celled tumours are by no means confined to bone ; in fact cases now have been reported from many regions of the body, and next to the multiple osseous form the most common situation appears to be the nasopharyngeal, including the buccal cavity[8] and larynx. Here the growths may be pedunculated, sessile, or infiltrative[17, 18] in character, most if not all are locally malignant, and a few give rise to glandular metastasis. Claiborn and Ferris[19] point out that the average age is 47 years, that 84 per cent are males, and that the presenting symptom in 75 per cent of cases is nasal obstruction, the rest complaining of epistaxis, dysphagia, hoarseness, or swelling in the neck. The prognosis is far better than that of sarcoma, for which it is usually mistaken, local excision giving satisfactory results in most cases, though there is on record one patient in whom multiple myelomatosis developed eight years after tonsillectomy for plasmoma.[20]

Other cases have been reported from the conjunctiva,[21] the pleura,[22] the bowel,[23] the skin,[24] and also as a cause of enlargement of multiple lymphatic glands.[25]

When arising in bone it, together with neoplasia of blood-forming cells and marrow endothelioma, forms the group known as ' myeloma ', in which in days gone by osteoclastomata and even some osteogenic sarcomata were placed.

Geschickter and Copeland,[26] in their excellent analysis of 425 cases of multiple myeloma, point out that the plasma cell is the neoplastic element in about half

Site.—Every case except one, which arose in the great trochanter and spread along the neck of the femur to the acetabulum, originated in the shaft of a long bone. In this respect plasmocytoma resembles an endothelioma, but the latter

FIG. 506.—Microphotograph of section from plasmocytoma of the tibia.
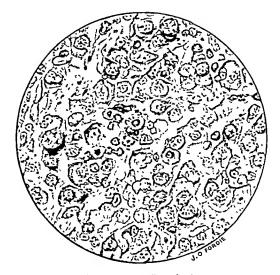
FIG. 507.—Drawing to show cells stained by Pappenheim's method for plasma cells.

tends to present as a low-grade osteomyelitis and occurs in younger subjects. Osteogenic sarcoma and osteoclastoma occur practically invariably at the meta-physial and epiphysial regions respectively.

Pathological Fracture.—This occurred in 12 of the 13 cases, it was the reason for seeking medical attention in 10, and is the outstanding characteristic. It occurs frequently in telangiectatic bone sarcoma,[31] but the young age, rapid growth, early metastasis, and fatal termination make the diagnosis clear. Some 13 per cent of osteoclastoma show this condition, but the large swelling and the site of origin are distinctive.[32] Osteitis fibrosa cystica is commonly associated with pathological fracture, but the localized form is only found in youth.

Radiological Appearance.—This condition presents two distinct types of radiological appearance, both exceedingly suggestive. From those records in which it is possible to gather the appearance the commonest type is a solitary cyst in the shaft of a long bone. Extension takes place markedly in the long axis of the bone compared with the transverse, and neither periosteal nor osteogenic reaction is ever found. The second type shows a radiogram indistinguishable from that of an osteoclastoma, except that the site is different, which gives a clue to the diagnosis. Pathological fracture is almost invariably present in both. In the first group the age of the patient, and erosion rather than expansion, differentiate it from osteitis fibrosa cystica. Endothelial myeloma shows a periosteal reaction but no cyst formation, while endosteal sarcoma tends to present relatively less axial extension, greater lack of definition in the area of rarefication, and an osteogenic reaction may be present. In secondary carcinoma metastases from the thyroid and hypernephroma give rise to a shadow that is very similar, but the spread is more centrifugal; the diagnosis must be clinched by the clinical findings of the primary growth or noting the great vascularity or even expansile pulsation of the bone lesion.

Histological Appearance.—This is the only certain method of making the diagnosis, though it is of interest to record that with the exception of endothelial myeloma I have been unable to find any other type of solitary myeloma of long bone in the literature. Myelocytoma is occasionally found as a solitary lesion in the spine or skull, but erythroblastoma and lymphocytoma are apparently only found in the diffuse form of multiple myelomatosis. Sections show plasma cells of varying size with mitotic figures amongst them.

RÉSUMÉ OF TREATMENT AND PROGNOSIS IN RECORDED CASES

Deep X-ray Therapy.—This has been tried in three cases :—

1. Successful : a femur ; the only case in the series without a pathological fracture ; alive, well, and with no disability three years later.[6]

2. Failure : a humerus ; radiation was combined with Coley's fluid ; retrogression occurred at first, but as there was no tendency for the pathological fracture to heal amputation was resorted to with success.[6]

3. Failure : a femur, which four months before had been cauterized with the electric cautery and the cavity wiped out with 50 per cent zinc chloride and had had two pathological fractures since operation, was brought back for radiation and Coley's fluid. The report stated that he was " gradually loosing ground ".[5] It should be noted in passing that plasma-celled tumours are not radio-sensitive in other situations, possibly because they are the cell associated so frequently with chronic inflammation.[32, 33]

Radium.—This was tried in one case,[4] but unfortunately sepsis supervened and amputation became necessary. On post-operative examination of the femur no trace of the growth could be found, its situation being replaced by fibrous tissue.

Conservative Surgery.—There were three cases in this group :—

1. Successful : a humerus treated by curettage and bone-graft from the tibia, the patient being alive, well, and with no disability one year later.[2]

2 and 3. Failure : the femur was involved in both cases and treated by curettage without graft.[5,10] One is mentioned above as having post-operative radiation, and the other died of cirrhosis of the liver four months later without signs of local improvement.

Radical Surgery.—Amputation was performed in 6 cases, and 4 of the patients were reported as alive and well from a few months to eight years later. Successful cases were : humerus[6,8] (2), femur[4] (1), and tibia (1). Two cases with involvement of the femur died of operative shock following disarticulation through the hip-joint.[3,7]

Results.—Two patients died of operative shock, one of ? pneumonia,[1] one of perforated duodenal ulcer,[9] one of cirrhosis of the liver,[10] one of cerebral hæmorrhage.[11] Of the 7 remaining alive, 6 were reported well, but the seventh had signs of local recurrence.[5] In no case did multiple myelomatosis develop, though this has been recorded when the original lesion was in flat bones.

SUMMARY

1. A case of solitary plasmocytoma of the tibia is recorded for the first time.

2. The condition is discussed after analysis of the 12 recorded cases.

3. Every case of primary tumour of the shaft of a long bone should have a biopsy performed in case it is a myeloma, and if found to be of endothelial origin treated by deep X rays, and if a plasmocytoma by curettage and bone-graft.

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THE BLADDER FUNCTION IN SPINAL INJURY*

By KENNETH H. WATKINS

HONORARY ASSISTANT SURGEON, MANCHESTER NORTHERN HOSPITAL

OPINION is by no means unanimous on the behaviour of the urinary bladder following disturbances of its innervation. It is, however, commonly believed that the bladder still exhibits a considerable activity even after its complete isolation from the central nervous system. On this view the importance of the peripheral nerve ganglia as 'centres' for micturition has been repeatedly emphasized.

This work was undertaken in an attempt to determine the exact function which exists in the bladder in cases of injury to the sacral segments of the spinal cord or cauda equina. More recently opportunity has occurred to study the behaviour of the bladder in cases of complete transverse lesions of the spinal cord. In these cases the influence on the bladder of the intact sacral segments of the spinal cord has been observed.

The Innervation of the Bladder.— The urinary bladder receives its nerve supply bilaterally from two sources (*Fig. 508*). These are the hypogastric nerves of the sympathetic nervous system, and the pelvic nerves (nervi erigentes) of the sacral parasympathetic outflow. The act of micturition is, however, importantly influenced by a third factor, the striated muscle of the sphincter mechanism, innervated by the internal pudic nerves.

FIG. 508.—The innervation of the bladder. (*Modified from Professor J. R. Learmonth, 'Proc. Staff Meetings Mayo Clinic', 1931, vi, 182.*)

The nerve-fibres of the sympathetic system proceed to the hypogastric nerves by various routes. In man the connector cells of origin are situated in the lower thoracic and upper lumbar segments of the spinal cord (about ninth thoracic to second lumbar). Their fibres pass to the lateral sympathetic chain, and from there the greater number reach the presacral nerve of Latarjet, which lies in front of the body of the fifth lumbar vertebra. This nerve divides at its lower end into the right and left hypogastric nerves. The hypogastric nerve passes on each side to the hypogastric ganglion, from which the fibres proceed to the pelvic viscera, including

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the wall and neck of the bladder. Some sympathetic fibres leave the sacral part of the lateral sympathetic chain and pass directly to the hypogastric nerve, and to the hypogastric ganglion (Latarjet and Bonnet,[6] Learmonth,[7] et al.).

The pelvic nerves (nervi erigentes) arise from the anterior divisions of the third and fourth sacral nerves. Latarjet and Bonnet[6] were not able to trace any connection with the second sacral nerves, but Learmonth[8] has evidence that the latter may sometimes play a part in the innervation of the bladder. Like the hypogastric nerves, the pelvic nerves also pass to the hypogastric ganglia.

The internal pudic nerves take origin from the second, third, and fourth sacral nerves, but, according to Rochet and Latarjet,[9] the striated fibres of the sphincter urethræ are suppplied chiefly by the third and fourth sacral elements.

It follows from this description that destruction of the third and fourth sacral segments alone will in most cases completely cut off the bladder from its innervation by the pelvic and pudic nerves, and leave it with its sympathetic (hypogastric) innervation alone.

Methods of Investigation.—Of the routine urological procedures no mention is necessary. It is essential, however, to refer to the technique of bladder pressure estimations, and to describe the findings in cases with a normal innervation. In this investigation a long vertical glass tube of about 4 mm. internal diameter was employed as the manometer. This was connected by a T piece with an inlying catheter and with a graduated reservoir for the introduction of fluid. The crest of the pubis, with the patient recumbent, was regarded as the 'zero' level. Two series of pressures were observed after each addition of 25 or 50 c.c. of fluid—those as the patient lay at rest, and again when he attempted to pass urine (Watkins[12]).
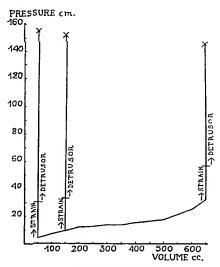
FIG. 509.—Bladder pressures in a case with normal innervation.

The characters of a bladder with normal innervation are shown in *Fig.* 509. The curve of the pressure as this man lay at rest shows a gradual rise as the volume within the bladder increases. His first sensation of anything within the bladder occurred with the introduction of 150 c.c. of fluid. On each occasion that he was asked to pass his urine the pressure increased rapidly by about 25 cm., and after an interval gradually and steadily to about 150 cm.; fluid was simultaneously voided around the catheter. The initial small rise of pressure is due to straining with the abdominal muscles, but the high pressure is the result of contraction of the detrusor muscle. Escape of fluid around the catheter is due to the associated reflex relaxation of the urethra.

Another example of normal innervation is shown in *Fig.* 510. When this man attempted to pass urine the resulting rise of pressure was usually only 3 to 5 cm., except at a capacity of 300 c.c., when reflex micturition was released, the pressure rising to 153 cm., and fluid being simultaneously passed around the catheter.

Recorded in the figures are also the pressures (47 and 34 cm.) which resulted when this patient was instructed to force as hard as possible with his abdominal muscles. These observations explain a type of pressure curve which is frequently found in bladders with normal innervation (*Fig.* 511). Here none of the earlier attempts to pass urine has released detrusor contraction, but the patient has increased the intravesical pressure to between 30 and 50 cm. by straining with his abdominal muscles as was apparent on watching his efforts. Only after the introduction of 600 c.c. did this man release a true detrusor contraction, the pressure rising to more than 150 cm.

Normal Micturition.—The two essential features of normal micturition are very clearly demonstrated by the above observations. Thus contraction of the detrusor muscle was shown to be very powerful, and promoted an intravesical
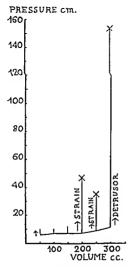
FIG. 510.—Bladder pressures in a case with normal innervation.
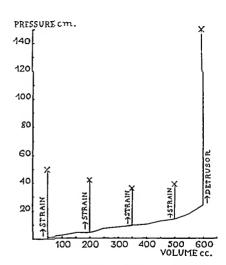
FIG. 511.—Bladder pressures in a case with normal innervation.

pressure much greater than that which could be achieved by straining with the abdominal muscles alone. The escape of fluid around the catheter revealed the associated relaxation of the sphincter muscles. It became very evident during observations on the normal bladder that abdominal straining plays no essential part in normal micturition. The difficulty which the normal individual may at times experience in releasing the micturition reflex was also very apparent. It proved that micturition could not be initiated in a manner comparable to the voluntary movement, for example, of a limb, and gave rise to the idea that voluntary micturition was dependent upon 'facilitation' within the central nervous system. Denny-Brown and Graeme Robertson[3] have evidence that it is more accurately to be regarded as due to the removal of an inhibitory suppression of the micturition reflex.

CASE REPORTS

Case 1.—**Hæmatomyelia of the conus medullaris.**—

G. C., aged 19, was admitted to the Manchester Royal Infirmary on Feb. 24, 1928, under the care of Professor A. H. Burgess, who subsequently referred the case to Mr. Jefferson.

He had fallen a distance of 25 ft. from some scaffolding and had sustained a severe injury to his back. He was found to have a compression fracture of the first lumbar vertebra, with an injury to the conus medullaris.

Examination.—There was no paralysis or weakness of the muscles of the limbs. The knee-jerks were active and the ankle-jerks absent. There was a ' saddle ' area of dense anæsthesia extending on to the posterior aspect of the scrotum. (This was more extensive than is indicated in *Fig.* 512, made at a later date.) Sphincter ani completely relaxed.

Bladder Function.—Retention of urine was absolute and was treated at first by intermittent catheterization and later with an inlying catheter.

Bowel Function.—No control.

On April 1, 1928, it was observed that the ankle-jerks had recovered, the left being more active than the right. One day during the later part of April (about two months after the injury) the inlying catheter became dislodged and the patient found to his surprise that he was able to pass some urine. He continued subsequently without recourse to catheterization.

On June 25, 1928, this patient attended as an out-patient.

Bladder Function.—There was no control at all during the night time, whilst during the day he could hold the urine for as long as two hours, though at times he might have to pass it every fifteen minutes.

On Oct. 5, 1931, he reported that he was working as a brick-building labourer.

Bladder Function.—He stated that the urinary stream was of very poor force, that it was frequently interrupted, and that sometimes it occurred only in drops. Incontinence at night time continued, and on most days he wet himself a little, always keeping a pad to soak up the urine which escaped. But he was quite certain that he could avoid incontinence completely during the day if he always went to urinate as soon as he felt the desire. A variable degree of frequency was still present, though often he would be able to hold his urine for three hours.

Bowel Function.—There was marked constipation and frequent soiling of the clothes from the passing of flatus.

The Act of Urination.—The patient had not passed any urine for two hours and yet was unable to urinate on request. Firm pressure was made in the hypogastrium in an attempt to express urine. But although this was not successful it did promote the desire to urinate, and he then passed about 75 c.c. of urine in an interrupted stream. At first a few drops appeared, then a short stream, another few drops, another stream, and so on. The streams were of poor force.

Residual Urine.—This was found to be 300 c.c. immediately after the above act of urination. A considerable quantity of the urine was spontaneously evacuated through the catheter, but the latter part did not empty until after the application of pressure to the hypogastrium.

Cystography.—Sodium iodide (5 per cent) was introduced into the bladder, and skiagrams were taken immediately, and again after partial emptying of the bladder by catheter. This examination demonstrated a great degree of irregularity of the bladder and relaxation of the vesical orifice, the so-called ' funnel ' urethra (*Fig.* 513). There is, however, no gross relaxation of the vesical orifice in the film made after partial emptying (*Fig.* 514). Regurgitation occurred up the right ureter and demonstrated a hydronephrosis and hydro-ureter on that side.

On Oct. 25, 1931, the patient felt so much improved that he had given up wearing pads to absorb urine.

Bladder Pressure Estimations.—After introducing a bicoudé catheter it was noticed as before that the last portion of the urine did not escape until assisted, on this occasion by straining efforts on the part of the patient, which resulted in the expulsion of another 50 c.c. or more of urine. The bladder-pressure curve (*Fig.* 515) exhibited some unusual features. The curve of ' rest ' was an extremely steep one, and the first sensation of filling was noticed with only 75 c.c. of fluid in the bladder. The capacity, as indicated by the point of severe discomfort, was only 175 c.c., although the residual urine had previously been found to be

FIG. 512.
Case 1. Sept. 18.
1935.

300 c.c.   The pressures of 'attempted urination' were only 20 to 30 cm. greater than those of 'rest' and did not show any evidence of normal contraction of the detrusor.

On Jan. 23, 1933, he reported that he was in excellent health.

Bladder Function.—It was usually necessary to strain much harder than normally to urinate, though sometimes if desire was actually present the urine might come fairly easily.

FIG. 513.—*Case* 1.   Cystogram (first film).
Oct. 5, 1931.

FIG. 514.—*Case* 1.   Cystogram (second film).
Oct. 5, 1931.

As a rule the urinary stream was interrupted many times, and there was marked terminal dribbling.   The patient stated quite definitely that he could keep himself entirely dry by always responding quickly to the desire to urinate.   However, he preferred to wear an apparatus to catch the urine whenever he left his home.   Incontinence always occurred at night.   He usually passed urine six or seven times during the day, and could hold it for as long as four hours at a time.

FIG. 515.—*Case* 1.
Bladder pressures.
Oct. 25, 1931.

Bowel Function.—Constipation was now less troublesome, but some incontinence still persisted; there was a tendency to soil a little from the passage of flatus or when attempting to urinate.

The Act of Urination.—On being requested to urinate this patient strained very hard, and contracted his abdominal muscles strongly.   There resulted a stream of poor size and force, and this ceased instantly when the effort of straining was relaxed in order to take a deep breath.

Urine.—The urine was moderately cloudy and contained many leucocytes and some epithelial cells.

On Aug. 22, 1934, this patient reported again, complaining of abdominal pain, malaise, and more frequent urination with more troublesome incontinence of eight weeks' duration.   Previously he had been doing splendidly.   He would pass his urine six or seven times every day and would never get more than a very little wet in between times.   Frequently he would wear an apparatus to catch what did come away, but at other times he would not trouble to use it even when going some considerable distance from home.   At night time he was always incontinent.   He stated that his urinary stream was interrupted.   Examination revealed an abscess in the lower abdomen, which had apparently taken origin from one of the small diverticula of the bladder.   After the abscess had been drained through a lower abdominal

incision urine leaked from the wound. Healing occurred with the help of an inlying catheter. During his stay in hospital (when he was bed-ridden) he had been persistently incontinent of both urine and fæces.

Cystoscopy.—The examination was made under ether anæsthesia with the concave sheath. There was a considerable amount of debris within the bladder. Trabeculation was considerable. The muscle bundles seemed to be fewer in number than is the case in obstructive conditions but they were very much more prominent and projected more markedly within the bladder cavity. Numerous orifices of diverticula were present. The ureteric orifices appeared normal. The vesical orifice was seen to be widely open, and one could examine the whole extent of the posterior urethra with the concave sheath.

On March 9, 1935, he had put on a stone in weight and was feeling fine.

Cystography.—A 15 Charrière rubber catheter was passed and readily entered the bladder. About 200 c.c. of 5 per cent sodium iodide was run into the bladder rapidly under a pressure of about 60 cm. This caused some discomfort, and a moment later the catheter slipped out of the bladder, followed by a little of the fluid. A skiagram was made when the fluid had ceased to run. A second film was made about thirty minutes later, at which time the patient was experiencing a good deal of smarting in the bladder. He then passed about 50 c.c. fluid, and another film was made three or four minutes later. The first two films showed wide relaxation of the internal sphincter and posterior urethra (*Fig.* 516), whilst in the third film no contrast medium could be seen in the posterior urethra (*Fig.* 517). The broad projection below the main bladder shadow seen in *Fig.* 517 is evidently a pouch from the bladder base. It can also be seen in the other films, in which it is partly superimposed upon the shadow of the dilated posterior urethra.

On Sept. 18, 1935 (seven and a half years after the accident), he reported himself as being very well.

FIG 516 —*Case* 1. Cystogram (first film). March 9, 1935.

FIG. 517.—*Case* 1. Cystogram (third film) March 9, 1935.

Bladder Function.—Sometimes he wears an apparatus and at other times just something in his trousers to soak up the urine. His urination varies greatly. He may occasionally be several hours without passing urine. At other times he may have to go three times within a few minutes. When he is incontinent he is certain that it is only small quantities at a time. As before, he can keep himself practically dry provided he is near a lavatory all

the time so that he can answer the call immediately.   At night time he always keeps a bottle in bed and does not wake up.

Bowel Function.—Very constipated.   He loses control if he has diarrhœa.

Examination.—Motor power excellent.   Knee-jerks, active ; ankle-jerks, left not quite as active as the right.   There is a saddle area of diminished sensation to pinprick extending on to the back of the scrotum (*see Fig.* 512).   Anal sphincter entirely patulous.

FIG. 518.—*Case* 1.   Cystogram (second film).
Sept. 18, 1935.

FIG. 519.—*Case* 1.   Cystogram (fourth film).
Sept. 18, 1935.

Combined Pressure Observations and Cystography.—He passed 100 c.c. of fairly clear urine.   A rubber catheter (18 Charrière) entered the bladder readily and evacuated 170 c.c. of urine.   Sodium iodide 5 per cent was introduced at a pressure of just over 80 cm. and the fluid was allowed to run in at full speed until he began to complain of the bladder being full, which occurred at a capacity of about 200 c.c.   The inflow was stopped at 200 c.c. and the first X-ray was taken, the level in the manometer having fallen from that of introduction to a pressure of 60 cm.   The pressure was then observed to fluctuate at intervals, e.g., from 40 to 65 cm., and then from 40 to 52 cm.   The second film was taken when the pressure registered 38 cm. immediately after the pressure had fallen to this level following a contraction.   Subsequent to this the pressure fluctuated from 38 cm. up to 65 cm. and down to 38 cm. again, and then up to 53 cm.   In both these films (*Fig.* 518) there was the widest degree of relaxation of the vesical orifice and posterior urethra : 85 c.c. was then removed from the bladder, and the intravesical pressure registered 16 cm.   A third film was taken at this pressure.   After this the pressure was observed to fluctuate again from 16 cm. up to 35 cm. and back to 16 cm. up to 23 cm. and then back again.   The fourth film was made when the patient again attempted to pass urine, and the pressure rose to 43 cm., the film being taken just as it had started to fall and registered 38 cm.   In these two films there is relaxation of the vesical orifice and posterior urethra, but to a lesser degree than in the first films (*Fig.* 519).

Comment.—After a period of acute urinary retention following injury to the conus medullaris this patient developed a remarkable degree of control over his bladder function.   The condition after seven and a half years shows that this was not due to recovery on the part of the innervation itself.

Case 2.—Injury to the cauda equina.—

W. C., aged 35, was admitted to the Salford Royal Hospital on Sept. 22, 1930, under the care of Mr. James B. Macalpine. Ten days previously, when he was working down a coal mine in a crouching attitude, he had been struck on the back by a heavy mass. He stated that his only complaint at first was that there seemed to be no sensation when his bladder was full, and that he only passed his urine once a day. However, two days before his admission to hospital, he felt a severe pain in his back when his nurse lifted him up in bed, and from that time urinary retention had been complete.

Examination.—X-ray examination revealed a forward displacement of the fifth lumbar vertebra on the sacrum. All the muscles below the knees were weak with the exception of the right tibialis anticus. The left tibialis anticus acted less strongly than the right, but the long flexors and extensors of the ankles and toes did not show any action at all. All the other muscles were acting with the exception of the glutei. The knee-jerks were active and the ankle-jerks absent. There was an area of complete anæsthesia over the 'saddle' region, extending down the backs of both thighs and on to the penis and scrotum (*Fig.* 520). Sphincter ani entirely relaxed.

Bladder Function.—The complete retention of urine was at first treated by regular catheterization, but subsequently an inlying catheter was employed. A fairly bad cystitis developed at this time.

Bowel Function.—No control.

Fig. 520.
Case 2. Sept. 14,
1935.

Cystogram (Oct. 3, 1930).—There was no evidence of a 'funnel' urethra or other abnormality at this time (*Fig.* 521).

On Nov. 14, 1930, some urine was voided for the first time, and three days later the residual urine was found to be 500 c.c.

Fig 521.—*Case* 2 Cystogram.
Oct. 3, 1930

Fig. 522.—*Case* 2 Cystogram.
Nov. 10, 1931.

On Nov. 10, 1931, the patient reported for observation.

Bladder Function.—He stated that the urinary stream was only of moderate force. Occasionally slight incontinence of urine occurred, but he had not wet himself for the past two weeks. He could hold his urine for two or three hours at a time, but at night he kept a urinal in bed.

The Act of Urination.—He was observed to strain very hard, and was only successful after an interval. He then passed some urine in an interrupted stream, which was fine and of only moderate force.

Cystography.—This showed a very marked degree of irregularity of the bladder wall, and relaxation of the bladder neck or 'funnel' urethra (*Fig. 522*).

On Jan. 1, 1932, this patient again reported for observation.

Bladder Function.—He thought his urine was passing with less difficulty than before. He stated that it passed in a fairly good stream with some dribbling. With care there was no incontinence at all during the day, but if he neglected for long the desire to urinate a little would come away of itself. He still kept a urinal in bed. In the daytime he passed urine every hour or two but could sometimes hold it for three hours.

On Jan. 12, 1933, he stated that his general health was excellent.

Bladder Function.—This had improved very considerably. He thought that he did not have to strain quite so hard as before, but straining was a very definite factor, and, as he himself remarked, he never had to strain at all before his accident. Often he had to wait some time before the urine would come, and the stream was always interrupted several times and there was terminal dribbling. If he neglected to respond quickly to the sensation of bladder fullness, some incontinence would ensue ; and if somebody made him laugh when his bladder was full, a few drops of urine would escape. But with care he was able to keep himself free from incontinence both by day and night. He passed urine five or six times every day, and always two or three times at night. The amount of urine would show much variation, being sometimes large but at other times quite small.

Bowel Function.—He had not complete control of his bowels, and straining to urinate was liable to cause some fæces to pass. He also required frequent purgatives to work the bowels.

FIG. 523.—*Case* 2. Bladder pressures.
Jan. 12, 1933.

The Act of Urination.—The urine was passed in a series of small streams of fine calibre, and it was observed that the interruptions between the streams corresponded exactly with the times at which the patient paused in his straining efforts in order to take a deep breath. About 175 c.c. of urine was passed with about twelve interruptions of the stream.

Residual Urine.—This was found to be 200 c.c. The catheter was apparently not detected in the anterior urethra but it was felt as it approached the bladder neck.

Urine.—The urine was slightly cloudy and contained many leucocytes and Gram-positive cocci.

On Nov. 4, 1933, he again reported for observation.

Bladder Function.—He must always strain to pass his urine. If his bladder was very full, he said he did not have to strain very hard. And when his bladder was full he thought the urine came in a continuous stream, so long as he strained all the time. But otherwise the stream was always interrupted. Some terminal dribbling. Sometimes there was a very marked urgency, but at other times he could wait half an hour after the sensation first came on. He had not wet himself for several months now, either during the daytime or at night. Sometimes he passed urine every two hours, but often could hold it as long as four hours. Usually passed it twice every night.

Sexual.—Erections do occur, but not so strongly. Has been having intercourse but it is not satisfactory. Uncertain about ejaculations, but at one time urine would come from him.

The Act of Urination.—There was much straining so that he became very red in the face. The urinary stream was interrupted many times, and the interruptions occurred exactly whenever he took a deep breath. He passed 125 c.c., about 10 c.c. at a time, in a narrow stream of poor force.

Residual Urine.—This was 40 c.c., and it was necessary to express the urine by pressure applied to the hypogastrium.

Bladder Pressure Estimations (Fig. 523).—The first sensation from filling of the bladder was appreciated at 250 c.c. Each attempt at urination was associated with great effort of straining, and no evidence of powerful detrusor contraction was found.

Combined Pressure Observations and Cystography (Feb. 23, 1935).—Sodium iodide (5 per cent) was used. After passing a rubber catheter 150 c.c. of fluid was evacuated with the aid of pressure in the hypogastrium. Contrast medium was quickly run into the bladder and at 150 c.c. he noticed the sensation, and at 220 c.c. he experienced pain. The inflow was then closed and the first film was taken with the pressure at 28 cm. After an interval of some minutes the pressure had subsided to between 5 and 8 cm. at which point the second skiagram was made. The noteworthy point about these films (which are similar to those at a later date (*see Fig.* 524) is that they show a bladder of relatively smooth outline as compared with the cystogram of 1931 (*see Fig.* 522), and that there is no evidence of relaxation of the internal sphincter. It should be noted also that the bladder pressures did not rise higher than 28 cm. of water, in spite of the very rapid introduction of fluid.

Residual Urine (March 13, 1935).—230 c.c.

The man was next examined on Sept. 14, 1935, five years after the original injury.

Bladder Function.—He could now hold his urine as long as six hours in the night. He was still conscious of the necessity to strain to pass urine. He was not troubled by incontinence at all.

Bowel Function.—No control when bowels are loose. Constipated; taking purgatives twice a week.

Sexual.—He says his erections are improving, though not perfect. Intercourse is not very satisfactory on account of the anæsthesia, but he does get an orgasm.

Examination.—Movements of the right leg and foot good. Left leg wasted below the knee. Cannot move any of the toes of this foot. He can dorsiflex and plantarflex the foot moderately strongly.

Knee-jerks: Right active, left exaggerated. Both ankle-jerks absent. There is complete loss of sensation to pinprick over the 'saddle' area, backs of both thighs as far as the knee-joints, scrotum, and penis (*see Fig.* 520). No tonus can be detected in the sphincter ani.

Act of Urination.—He was wanting to pass urine after being given a large quantity of water to drink. He now passed 500 c.c. urine. The first part came in a good strong stream of quite good calibre, but the latter half was very much interrupted, and there was some straining. But even with this part

FIG. 524.—*Case* 2. Cystogram. Sept. 14, 1935.

the force was fairly good, and the interruption was partly due to the manipulation of the penis with his fingers as a sort of 'milking' effect which seemed to help him to pass it.

Residual Urine.—150 c.c.

Combined Pressure Observation and Cystogram.—Sodium iodide 5 per cent was used. The fluid was introduced rapidly under a pressure of about 60 cm. The patient felt uncomfortable after the introduction of 250 c.c., and at 330 c.c. the inflow was stopped. The first X-ray was then taken, the pressure being 22 cm. water. After a minute or two the pressure was 11 cm. and a second X-ray was taken. He then attempted to pass urine, but only succeeded in raising the pressure to 40 or 50 cm., the third film being taken at the height of straining. In all these films the appearances were identical—smooth bladder outline without any evidence of weakness of the vesical orifice (even when the patient attempted to pass urine) (*Fig.* 524).

Comment.—The condition of the bladder in this case of injury to the sacral nerves was at first similar to that in *Case* 1. It is clear, however, that recovery of the bladder function had been taking place very gradually. Urinary incontinence

ceased to occur, and at the last observation urine was passed in a good strong stream, though emptying was still incomplete. The cystogram at the end of fourteen months showed gross irregularity of outline and marked relaxation of the vesical orifice ; but these abnormal appearances were no longer present after five and a half years. The bladder pressure estimations were made three years after the injury, and it is probably also on account of commencing recovery that the curve was not as steep as might have been anticipated by comparison with *Cases* 1 and 5.

Case 3.—**Injury to the cauda equina.**—

W. McG., aged 7, was admitted to the Stockport Infirmary on April 7, 1930. He had been knocked down by a motor-car and sustained a fracture dislocation of the fifth lumbar vertebra, which was displaced backwards.

Examination.—There was no paralysis or weakness in the limbs. Knee-jerks active ; ankle-jerks and plantar responses absent. There was loss of sensation extending over the ' saddle ' area, down the backs of both thighs, and over the lateral parts of the legs and feet. (More extensive than is shown in *Fig.* 525, which represents a later date.)

FIG. 525.
Case 3. Nov. 21, 1933.

Bladder Function.—Retention of urine was present, and was treated by intermittent catheterization.

Bowel Function.—There was complete incontinence of fæces.

This patient was transferred to the Manchester Royal Infirmary under the care of Mr. G. Jefferson, and a laminectomy was performed on May 21, 1930. The dural sac showed a definite level of compression at the junction of the fourth and fifth lumbar vertebræ, and the arachnoid space was obliterated there. The nerve-roots were unruptured but rather gummy-looking below the compression. Recovery from the operative procedure was uneventful.

On July 20, 1931, considerable improvement was reported.

Bladder Function.—He could hold his urine for at least several minutes after the perception of the desire. He was passing urine voluntarily about six times a day, and did not get up at night.

Sphincter Ani.—This was extremely relaxed, and it was possible to expose the rectal mucosa by gentle traction on the skin around the anus.

The Act of Urination.—On being requested to pass urine this patient was observed to strain hard and contract his abdominal muscles. A stream of poor force was produced, which ceased when he stopped straining. With further straining the stream started again, and was interrupted several times in a similar way.

Suprapubic Expression.—This caused urine to escape in a stream which was continued only so long as the pressure was constantly maintained. The bladder could be palpated two inches above the symphysis pubis.

On Aug. 18, 1931, this boy was re-admitted to the Manchester Royal Infirmary for observation.

Bladder Function.—Following instrumentation urination became more difficult, and on a few occasions the bladder became very distended ; the boy complained of severe pain, and was relieved by catheterization.

Cystography.—A large smooth bladder with a well-marked ' funnel ' urethra was demonstrated (*Figs.* 526–528).

Bladder Pressure Estimation (*Fig.* 529).—The curve ' at rest ' was not abnormal in type. The first sensation was of ' pain in the stomach ' at 300 c.c. The pressures of attempted urination were about 100 cm., and showed the features characteristic of abdominal straining.

On Jan. 1, 1932, further progress was reported.

Bladder Function.—He occasionally wet his shirt very slightly, and rarely also he wet his bed. He passed urine every two hours or so, and once in the night.

The Act of Urination.—He was observed to pass about 50 c.c. of urine in an interrupted stream of poor force. Subsequently the bladder was palpable at a level about two inches below the umbilicus.

FIG. 526.—*Case* 3. Cystogram (first film).
Sept. 7, 1931.

FIG. 527.—*Case* 3. Cystogram (second film).
Sept. 7, 1931.

FIG. 528.—*Case* 3. Cystogram (third film).
Sept. 7, 1931.

Suprapubic Expression.—Expelled urine in a stronger stream than was attained in urination. On Jan. 12, 1933, the boy reported for observation and was in excellent health.

Bladder Function.—He stated that the urinary stream was usually interrupted. During the day he occasionally wet his shirt a very little, whilst at night he might go two or three weeks without trouble; last week, however, he was incontinent on two occasions. He passed urine four or five times during the day, and once or twice every night.

The Act of Urination.—He was seen to pass 150 c.c. of urine in a stream which was interrupted about ten or twelve times whenever he ceased straining to draw a deep breath. (The bladder had been palpable two finger-breadths below the umbilicus.)

Suprapubic Expression.—Caused urine to escape only so long as the pressure was continued.

On Nov. 21, 1933, three and a half years after the injury, this boy was again examined.

Bladder Function.—On most days he wet himself a little, and sometimes quite a lot if he stayed out too long playing with other children. The frequency varied considerably, but he could hold his urine for as long as six hours.

Bowel Function.—Frequently his clothes were soiled after taking purgatives, but he did not have any accident as long as his motions were solid.

Examination.—Contour and movements of lower limbs normal. Knee-jerks both active; ankle-jerks absent. Loss of sensation over the 'saddle' area and down the backs of both thighs to the level of the knees (*see Fig.* 525). The anus admitted two fingers, and no tonus could be detected. The fundus of the bladder was palpable mid-way between the symphysis pubis and umbilicus.

The Act of Urination.—It was evident that he expelled his urine by abdominal straining. He passed 175 c.c. with seven or eight interruptions. Subsequently 25 c.c. was expelled by pressure applied to the hypogastrium.

Urine.—Centrifuged deposit contained occasional epithelial cells only.

FIG. 529.—*Case* 3. Bladder pressures. Aug., 1931.

Comment.—The type of urination in this case of injury to the cauda equina was similar to that of the other cases in that it was entirely dependent upon abdominal straining. Some important differences in the behaviour of the bladder, especially the absence of resistance to filling, will be discussed below.

Case 4.—Spina bifida with involvement of the sacral nerves.—
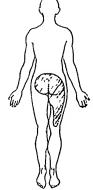
R. L., aged 10, was admitted to the Chirurgische Universitätsklinik, Freiburg im Breisgau, Germany, on Feb. 20, 1933. He had apparently been quite healthy until two and a half years before, since when he had developed bladder and rectal trouble. The condition was found to be due to spina bifida.

Bladder Function.—He passed urine about every two hours. Often there was a slight wetting of the clothes, but this was never very much. He was always incontinent at night. He always knew when he wanted to pass urine.

Bowel Function.—He had no control over his bowels.

Examination.—The boy walked perfectly. The contour of the lower limbs was normal. There was a pressure sore over the right gluteal region. Limb movements were normal. Both knee-jerks were active; the ankle-jerk was present on the left side, but absent on the right. There was a 'saddle' area of complete loss of sensation to pinprick extending on to perineum, scrotum, and penis. This also extended down the posterior aspect of the right thigh (*Fig.* 530). The anal sphincter was entirely relaxed, admitting three fingers. Rectum full of fæces.

FIG. 530 —*Case* 4. March, 1933

The Act of Urination.—This was associated with much straining, and about 200 c.c. of urine was passed in a narrow stream of poor force, which was interrupted each time that the taking of a deep breath interfered with the straining. The abdominal muscles could be felt to contract during straining.

Suprapubic Expression.—Pressed out urine fairly readily, but the flow ceased instantly on releasing the pressure.

Urine.—Contained a few leucocytes.

Cystoscopy.—Under light intravenous anæsthesia cystoscopy showed the mucous membrane of normal appearance. but the bladder neck was widely open so that the whole posterior urethra as far as the colliculus seminalis was readily seen.

Comment.—This case also demonstrates the typical behaviour of the bladder in lesions of the conus or cauda equina. The characteristic nature of the urinary stream and its dependence upon abdominal straining were very clearly demonstrated.

Case 5.—**Spina bifida with involvement of the sacral nerves.**—
W. N., aged 7, first attended the Brady Urological Institute at the Johns Hopkins Hospital on April 6, 1932, and was subsequently under observation there for several months. When six weeks old he had been operated upon for meningocele and spina bifida, and at the age of three months for hydrocephalus. The child had never been able to walk on account of extensive paralysis in the lower limbs, and incontinence of urine and fæces had been present since birth.

Bladder Function.—The mother stated that the urine escaped by a more or less continuous dribbling, and that it never seemed to come in an actual stream except occasionally when the boy laughed. There was no control whatsoever.

Bowel Function.—No control.

Examination.—The child was of poor intelligence. There was a small cranial defect in the parietal region, and an operative scar in the lower lumbar region. A deep pressure ulcer was present in each gluteal region. All the muscles below the knees, the hamstrings, and the glutei were paralysed on both sides. There was bilateral congenital dislocation of the hips, with contractures of hips and knees, and bilateral drop-foot.
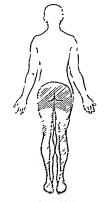
FIG. 531.
Case 5. April 6, 1932.

Both knee-jerks were active ; ankle-jerks absent. There was loss of sensation over the 'saddle' area, and the lateral surfaces of the legs and feet. Pinprick was appreciated to some extent over the posterior aspect of both thighs (*Fig.* 531). No anal sphincter tone could be detected. The rectal mucous membrane was readily exposed by means of very gentle traction on the skin.

Suprapubic Expression.—Urine (40 c.c.) was expressed without difficulty, the stream ceasing instantly on removing the pressure : 35 c.c. of urine was then found in the bladder. No leucocytes were to be found in the centrifuged urine.

Cystography (Fig. 532).—Showed a small ovoid bladder, without gross trabeculation. The vesical orifice was relaxed, the so-called 'funnel' urethra ; there was a filling defect in the lower part of the latter which suggested an enlarged verumontanum.

FIG. 532.—*Case 5.* Cystogram.
April, 1932.

Bladder Pressure Estimation (Fig. 533).—A 14F coudé catheter was employed. The curve was remarkably steep, so that a pressure of 37 cm. of water was recorded at a volume of 150 c.c. This degree of distension gave rise to discomfort, but not to actual pain.

Cystoscopy.—This was undertaken with a ' convex ' sheath. The bladder wall appeared normal and without trabeculation. The vesical orifice was relaxed and its posterior lip was prominent. The verumontanum appeared pedunculated and mobile, and was almost transparent in appearance. On either side of the posterior wall of the urethra there radiated from the base of the verumontanum three ridges, of which the lowest were directed transversely outwards, the uppermost obliquely upwards and outwards. Appearing like congenital valves of the posterior urethra, they were, however, not sufficiently prominent to give rise to obstruction.

PRESSURE cm.

FIG. 533.
Case 5. Bladder pressures.
April, 1932.

On two occasions urethral instrumentation was followed by urinary retention. Catheterization relieved this condition, 250 c.c. being evacuated the first time, and 150 c.c. the second time.

The mother was instructed to make the child strain at regular intervals in the hope that some degree of voluntary control might be effected. On July 18, 1932, the boy was observed whilst he strained to urinate, and a stream of poor force with two interruptions was noted. On Aug. 1, 1932, his mother stated that he could keep himself fairly dry if he strained at hourly intervals, but that he was completely incontinent at night.

Comment.—This boy of 7 years had had an extensive lesion of the cauda equina since birth. Up to the time at which he first came under observation the bladder condition was apparently one of more or less continuous dribbling. He was taught to gain some degree of control by straining with his abdominal muscles.

Case 6.—**Complete transverse spinal lesion.**—

M. H., a girl of 13 years, was admitted to the Manchester Royal Infirmary on July 9, 1932, because of pain in the back and loss of power in the legs. She became totally paralysed shortly after admission, with incontinence of urine and fæces. There was dense anæsthesia and complete paralysis below the eighth thoracic segment. An exploratory laminectomy was performed by Mr. Jefferson and Mr. Platt on Aug. 6, 1932, and revealed a sarcoma of the vertebral column. X-ray therapy was subsequently employed. The patient was examined on Nov. 13, 1933. The general health had remained good but complete paralysis and absolute anæsthesia had persisted below the level of the lesion (*Fig.* 534). There were deep pressure sores on the back.

The mother states that the child had absolutely no control whatsoever over urination, nor had she any knowledge of when the bladder was functioning. The mother did not know how often urination occurred, but she had observed the urine to come away in a strong stream and uninterrupted. She seemed to think that urination was sometimes brought on by movements. There was no control over the bowels.

Bladder Pressure Estimations.—A 14 Charrière rubber catheter was introduced and strapped to the thigh. There was rather more than 50 c.c. of cloudy urine in the bladder. Estimations of the intravesical pressure were made after the
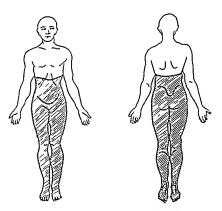
FIG. 534.—*Case* 6. Nov. 13, 1933.

introduction of each 50 c.c. of fluid. The volume of fluid which had been introduced did not always indicate the volume within the bladder since some fluid was evacuated alongside the catheter and only 200 c.c. of fluid was found in the bladder at the end of the examination (400 c.c having been introduced). After each introduction of 50 c.c. the pressure was watched over a period of several minutes.

VOLUME INTRODUCED	PRESSURE CHANGES
A few c.c.	After closing the inlet the pressure diminished slowly and at varying rates to 12 cm.
50 c.c.	Similar slow fluctuating fall to 29 cm., then a slight rise to 34 cm., falling to 23 cm., rising to 27 cm., and then falling to 12 cm.
100 c.c.	Fluctuating rates of fall to 19 cm., then to 16 cm., rising at a moderate and steady rate to 64 cm., falling in the usual fluctuating manner to 18 cm., and continuing again in a similar manner to 19 cm., to 17 cm., to 64 cm. by a steady rise, to 19 cm., to 43 cm., to 42 cm., to 60 cm.
150 c.c.	Fluctuating fall to 17 cm., steady rise to 68 cm., to 57 cm., to 69 cm., fluctuating fall to 24 cm., steady rise to 70 cm., to 38 cm., a small wave of contraction to 40 cm. interrupting the fall, which then continued to 17 cm. (*Fig.* 535).
200 c.c.	Fall to 16 cm., then up to 70 cm., to 59 cm., to 74 cm., to 24 cm.
300 c.c.	57 cm., to 69 cm., to 59 cm., to 66 cm., to 15 cm.
350 c.c.	42 cm., to 53 cm., to 42 cm., to 52 cm., to 36 cm., to 50 cm., to 17 cm.
400 c.c.	Fall to 18 cm.

The considerable rises of pressure which occurred always took place at a steady and fairly rapid rate. The fall of pressure always occurred much more slowly, at varying rates, and with short interruptions. Sometimes a small wave of increased pressure would interrupt the gradual fall. The pressure variations over a period of several minutes following the introduction of 150 c.c. fluid into the bladder are recorded in *Fig.* 535.

FIG. 535.—*Case* 6. Diagram of the pressure changes occurring spontaneously over a period of a few minutes. (Exact time not noted—about five minutes.) Nov. 13, 1933.

Comment.—Quite powerful and apparently spontaneous contractions of the detrusor muscle were occurring at intervals in this case of complete transverse spinal lesion at the eighth thoracic segment.

Case 7.—**Complete transverse spinal injury.**—

G. D. N., aged 23, was admitted to the Manchester Royal Infirmary on Nov. 21, 1933, under the care of Mr. Wilson Hey and of Mr. Geoffrey Jefferson. He had sustained an accident four weeks previously when he fell a distance of 40 ft. whilst rock climbing. He was found to have a compression fracture of the first lumbar vertebra with paralysis of the lower limbs.

Bladder Function.—He stated that he did not pass any urine after the accident until he was catheterized at the end of forty-eight hours. He did not get any pain from the over-distension of the bladder and he felt no sensation on catheterization. Intermittent catheterization was first employed, and subsequently an inlying catheter. On the fifteenth day, when the catheter became dislodged, urine seemed to come away from him easily on having his bowels well moved. From this time onwards he was not catheterized, and the urine seemed to run from him all the time.

Bowel Function.—For the first two weeks after the accident the bowels moved only with enemata. Since then they have moved once a day with fair regularity, but he has no control.

On abdominal examination (Nov. 28, 1933) the bladder felt like a ball extending two finger-breadths above the symphysis pubis. The application of pressure caused urine to be evacuated in a stream. On releasing the pressure the stream ceased, but a little dribbling followed for a moment or two. It was recorded at the time that the flow did not stop as immediately as is usual in cases of injury to the sacral segments. On Jan. 7, 1934, expression of the bladder showed just the same features, pressure causing a stream of urine, a little dribbling persisting after the removal of the pressure.

Examination.—The condition as observed on Aug. 12, 1934, is recorded here. At this time, almost ten months from the time of his accident, the level of sensory loss was practically the same as on admission. He was not able voluntarily to move toes, ankle, or knee on either side. He could flex at the hip-joint on the right side, but only quite weakly on the left side. Knee- and ankle-jerks were absent on both sides. Stimulation of the sole on the right side caused an upward movement of the toes with dorsiflexion and slight abduction of the ankle, and an upward movement of the toes on the opposite side. Stimulation of the toes on the left side caused an upward movement of the toes and dorsiflexion of the ankle on the same side.
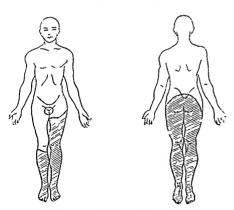
There was dense anæsthesia over the buttocks, backs of the thighs, legs, and feet (*Fig.* 536). The anæsthesia also extended over scrotum and penis.

Sphincter Ani.—One finger was passed and there was felt to be excellent tone (100 per cent). When a second finger was gradually introduced the tonus persisted at first and then very suddenly gave way, leaving the anus entirely patulous. On removing the fingers the mucous membrane of the rectum was now visible through a wide orifice. Approach of the finger to the anal canal produced a strong contraction of the anal sphincter immediately it made contact with the skin at the anus. (An active condition of the anal sphincter had previously been noted on April 5, 1934, at which time it was thought that movement of the finger within the anal canal promoted rhythmical contractions, which at their height seemed to be 100 per cent.)

Fig. 536.—*Case 7.* Aug. 12, 1934.

Bladder Function.—On Feb. 4, 1934, the passage of urine was watched over a period of two hours.

6.25 p.m.	Passed 55 c.c. in a continuous stream of moderate force and calibre, followed by a little terminal dribbling.
6.32 p.m.	He felt the sensation as if urine was passing, but no urine actually passed.
6.42 p.m.	Copious drinking of water commenced.
7.00 p.m.	Between 6.25 p.m. and 7 p.m. only one drop of urine had passed, and that just at the beginning of this period. He now felt the sensation which he associated with urination, and about ten seconds later passed 95 c.c. of urine in quite a good stream, with one interruption and a little terminal dribbling.
7.16 p.m.	A much stronger sensation occurred and about five seconds later he passed 85 c.c. in a quite strong stream with one interruption, followed by much terminal dribbling for about 15 seconds. When the penis was lifted to move the receiver a short spurt of urine occurred.
7.33 p.m.	Very quickly after the occurrence of the sensation he passed 130 c.c. in a good stream with one interruption.
7.36 p.m.	No response to stimulation of the penis with a pin.
7.42 p.m.	The sensation occurred followed quickly by the passage of 130 c.c. in a strong stream with one interruption.
7.43 p.m.	Attempted expression was unsuccessful. Quickly repeated sharp pressures in the hypogastrium were also without effect.
7.47 p.m.	Quickly repeated sharp pressures in the hypogastrium were followed by the sensation and then by the passage of 35 c.c. of urine in a stream of less than usual force. There was a short spurt, then a rather long interruption, and then another stream with one more interruption.

7.53 p.m.	Stimulation of the glans penis with a pin. After a moderately long latent interval 70 c.c. were passed in the usual way.
7.58 p.m.	Glans penis stimulated again. After 45 seconds he felt a weak sensation which recurred again after 60 seconds, but no urine escaped.
8.01 p.m.	The sensation occurred and five seconds later 125 c.c. passed with one interruption.
8.06 p.m.	Glans penis swabbed with methylated spirit. A small quantity of urine passed in small spurt.
8.07 p.m.	Swabbing glans penis was without effect.
8.10 p.m.	Glans penis swabbed again. After ten seconds he said, " It's coming ", and in another ten seconds there passed 110 c.c. in a strong stream.
8.17 p.m.	Bicoudé catheter passed. 140 c.c. urine evacuated from the bladder with the assistance of some pressure to the hypogastrium.

The urinary stream seen during the course of these observations seemed of normal force and calibre. The single interruption lasted one or two seconds and occurred when about half the urine had passed. The stream then came on again with its original force which became gradually less and finally passed into a little terminal dribbling.

Bladder Pressure Estimation.—On Feb. 13, 1934, a bladder pressure observation was made. On catheterization only a few cubic centimetres of urine were found in the bladder, and this was only evacuated with the help of pressure applied to the hypogastrium.

VOLUME INTRODUCED	PRESSURE CHANGES
A few c.c.	5 cm.
50 c.c.	The pressure fell to 30 cm. on closing the inlet, and then increased again gradually and in stages to 70 cm., and remained for a time fluctuating in this region, reaching a maximum of 85 cm. There was no associated straining.
60 c.c.	Pressure increased a little after closure of the inlet, and then gradually fell to 20 cm., during which time the patient complained of " aching in the kidneys ".
100 c.c.	After closing the inlet the pressure only fell a little to 72 cm., and then increased to 96 cm., fluid escaping simultaneously around the catheter.

This patient developed a severe urinary infection, and at one time it appeared likely that he would die from pyelonephritis. X-ray examinations revealed stones in both kidneys and on occasion small stones were passed. An excretory urogram showed dilatation of the pelvis and ureter on both sides. The latter examination also showed a small bladder of regular outline, but it did not provide definite evidence of the condition of the vesical orifice.

Comment.—In this case there was recovery of reflex activity in the segments distal to the crush. Observation of the urinary evacuations, which were involuntary, revealed an active condition of the bladder. The urine passed in a stream whose force and calibre were normal. The presence of powerful detrusor contractions was also confirmed by observations on the bladder pressure. There had, therefore, developed a high-grade reflex, though involuntary, micturition. There was evidence that micturition could be set up reflexly by certain forms of stimulation.

Case 8.—**Hæmatomyelia, with subsequent recovery of bladder function.**—
R. R., aged 50, was admitted to the Manchester Royal Infirmary on Aug. 13, 1931, under the care of Mr. C. Roberts. He had fallen a distance of 12 ft. and sustained a compression fracture of the first lumbar vertebra, with an injury to the lower spinal cord.

Examination.—On both sides all the muscles below the knee-joints were paralysed The quadriceps extensor and hamstring muscles were weak but not paralysed. Flexion, adduction, and abduction of both hips could be performed. Knee-jerks and ankle-jerks

were absent. Both lower limbs showed an extensive dense anæsthesia, the anterior and lateral surfaces of the thighs alone remaining unaffected, as shown in *Fig.* 537. The anus was without tone, and two fingers were readily introduced.
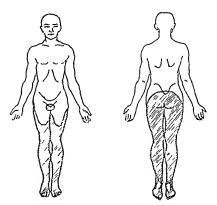
FIG. 537.—*Case* 8. Aug. 14, 1931.

Bladder Function.—Urinary retention was complete, and was treated by an inlying catheter.

Bowel Function.—There was no control.

Cystoscopy.—This was undertaken forty-eight hours after the accident. There was no trabeculation. No evidence of weakness of the bladder neck was observed, and the posterior urethra could not be brought into view with a ' concave ' sheath.

Cystography (Fig. 538).—Cystograms were made within twenty-four hours of the accident and on the 28th, 64th, 85th, and 132nd days. No evidence of weakness of the vesical neck could be found at any examination, even when unsuccessful efforts to urinate were made.

Bladder Pressure Examinations (Fig. 539).—During the early stage these observations were made on the 7th, 17th, 27th, and 54th days. All these curves were essentially similar. The capacity as indicated by severe discomfort varied between 550 and 650 c.c. Each curve of 'rest' showed a very gentle rise to a pressure of about 20 cm. of water at the full capacity. The curves of ' attempted urination ' were always low ; the greatest pressure attained was 87 cm. of water, but usually the pressure recorded was considerably less than this. The attempts to urinate were associated with very much straining, and the pressures could only be maintained momentarily. The first sensation of bladder filling was appreciated at these examinations with respective fillings of 400, 350, 250, and 200 c.c. The outstanding abnormal features at each examination were diminished appreciation of bladder filling and the absence of any sign of strong detrusor contraction.

Urine was first voided spontaneously on the 61st day, attempts on previous occasions having been without success. Occasional catheterization continued to be employed until the 75th day. Subsequently the passage of urine, which was at first a matter of extreme difficulty and associated with great effort, began to take place with increasing facility.

Residual Urine.—This was 550 c.c. on the 75th day. Subsequently it was estimated on a number of occasions to be rather more than 500 c.c. On the 116th day the residual urine was 300 c.c.

On the 116th day a bladder pressure estimation was made and certain remarkable differences from the previous examinations were evident. Pain was noticed after only 100 c.c. of fluid had been introduced into the bladder, and when 150 c.c. had entered

FIG. 538.—*Case* 8. Cystogram. Sept. 11, 1931.

the intravesical pressure overflowed the manometer (indicating a pressure of over 100 cm. of water) and urine escaped from the urethra alongside the catheter. These observations indicated improved bladder sensation, active detrusor contraction, and active relaxation of the urethra, and they demonstrated a returning function in the paralysed nerve-supply of the bladder.

A more complete series of observations were made on the 132nd and 133rd days.

Bladder Function.—The patient stated that he now usually passed urine every two hours during the day. When the desire to urinate was appreciated he could not wait for more than a very short time or it would come of itself. At night he wakened two or three times, and the urine came so rapidly then that he would wet the bed if he did not keep a urinal at hand.

Bowel Function.—This was now improved so that with suitable purgation the bowels moved once a day without incontinence.

Examination.—There was still almost complete paralysis below the knee-joints, excepting for some action of the left tibialis anticus. The hamstrings and glutei were very weak. The knee- and ankle-jerks were absent on both sides. The anal reflex was well marked from stimulation on either side. Pinprick was now appreciated as sharp all over the 'saddle' area. The posterior part of the right thigh was almost normal, but there was relative analgesia over the posterior part of the left thigh. Pinprick was definitely appreciated on the penis and scrotum. Gross anæsthesia to pinprick was present in both legs and feet up to the knee-joint on the left side, but not quite so high on the right side. The anal sphincter now showed definite tonus.
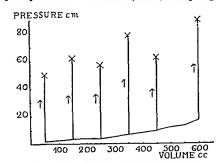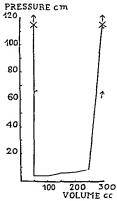
FIG. 539.—*Case 8.* Bladder pressures. Aug. 30, 1931.

The Act of Urination.—Whilst cleansing the glans penis preliminary to catheterization, urine was passed in a stream of considerable force with short interruptions. This action was quite involuntary. On the next day a similar phenomenon was observed when the penis was being examined by pinprick for analgesia. A sudden desire to urinate was aroused which passed off only after the passage of urine in an interrupted stream. After an interval of one minute the penis was again stimulated with a pin and after a few seconds desire to urinate was again manifested, and the interrupted stream was repeated. The abdominal muscles contracted strongly during the procedure but the whole process was apparently quite involuntary.

FIG. 540.
Case 8. Bladder pressures. Dec. 22, 1931.

Residual Urine.—On consecutive days this was found to be 300 c.c. and 175 c.c. respectively. All except the last few cubic centimetres was evacuated through the catheter in a strong stream.

Bladder Pressure Estimation.—In two consecutive examinations the curve of 'rest' was seen to be low and within normal limits. At the first examination, with 200 c.c. of fluid in the bladder, a sudden increase of intravesical pressure occurred so that the manometer overflowed (a pressure of more than 115 cm. of water). Bladder filling was appreciated with only 50 c.c. of fluid in the bladder. The result of 'attempted urination' was a pressure of over 115 cm. of water, even when there was only 20 c.c. of fluid in the bladder. At the second examination (*Fig.* 540) as the bladder filling was being increased from 250 to 300 c.c. a sudden rise of pressure occurred to over 115 cm. of water, and fluid was forcible expelled alongside the catheter. These observations confirmed those of the 116th day, demonstrating improved bladder sensation, active detrusor contraction, and active relaxation of the urethra.

The patient was next seen on Jan. 9, 1933, seventeen months after his accident. He reported a gradual steady improvement in his condition.

Bladder Function.—He stated that he did not have any further trouble whatsoever with bladder function. He did not now have to strain to urinate, and there was not any hesitation. He had not been troubled with incontinence at all since September, but when he first returned home this was a marked feature. The urinary stream was of good force and was not interrupted. Urine was usually passed five or six times a day, and he did not have to get up at night unless he took a large quantity of fluids in the evening.

Bowel Function.—He had complete control, and the bowels were moved regularly twice a day.

Sexual Function.—Occasional erections and nocturnal emissions occurred, and he thought that he would be able to perform sexual intercourse normally.

Examination.—He was quite unable to stand upright without support. There was marked wasting of the lower limbs. Abduction and extension of the hip-joints were weak. Quadriceps action was of only moderate power. Semimembranosus and semitendinosus were acting strongly, but no action of the biceps could be detected on either side. Practically no movements of ankles or toes could be undertaken except for a weak action of the left tibialis anticus. Knee-jerks were absent. Some ankle-clonus on both sides. Pressure over the anterior tibial muscles resulted in dorsiflexion of the toes on either side. Normal sensation was now present over the ' saddle ' area, the thighs, and the upper parts of the legs. There was still impairment of sensation in both feet and in the lower part of the left leg.

Comment.—Mr. Jefferson states that this must have been a scattered lesion of the spinal cord, with maximum damage to the fifth lumbar and first and second sacral segments.

It is very instructive to notice the different phases of bladder activity which were manifested in this case. The initial state was that of acute urinary retention. This passed on to a stage in which urination was evidently achieved by straining with the abdominal muscles which forced urine from a paralysed bladder. The extreme degree of effort associated with urination testified to that fact. Increasing facility of urination gradually developed, and the urinary stream regained a very considerable force. The evidence of this and of the bladder pressure observations showed that reflex micturition—powerful detrusor contractions associated with sphincter relaxation—had become re-established. For some long time, however, urinary control was absent, and the condition was one of involuntary reflex micturition as observed in the cases of transverse cord lesions, of which this was an incomplete example. Further evidence of the nature of the bladder function at that period is provided by the reflex facilitation of involuntary micturition which followed stimulation of the glans penis. At a still later time normal bladder function with perfect control became re-established.

DISCUSSION

BEHAVIOUR OF THE DETRUSOR MUSCLE

1. Lesions of Conus and Cauda Equina.—In striking contrast with the easy facility of normal urination, bladder emptying in these cases was a most laborious process. The efforts of straining were very considerable, and it was evident that the patient was utilizing his abdominal muscles to force out urine from the bladder. The urinary stream was interrupted at frequent intervals which always coincided with the moment at which the patient desisted in his straining efforts in order to take a deep breath. There can be no doubt that abdominal straining had replaced detrusor contraction as the expulsive force in urination. Furthermore, in no case did the observations on intravesical pressure reveal the powerful detrusor contraction characteristic of normal micturition. It can only be concluded that the detrusor muscle has lost its function of powerful contraction.

A surprising feature of these cases was the relatively small amount of fluid which could be injected into the bladder through a catheter. In *Case* 1 severe discomfort was produced by the introduction of 175 c.c. of fluid at a pressure of more than 60 cm., although there had been 300 c.c. of residual urine. This phenomenon was also observed in *Cases* 2 and 5.

The very steep curves of intravesical pressure, especially well marked in *Cases* I and 5 of this series, are manifestations of this same behaviour (*see Figs.* 515, 533). Both Schwarz[10] and Adler[1] were familiar with this type of curve in lesions of the conus and cauda equina. The explanation must be that the detrusor muscle reacts to rapid filling by a contraction which prevents distension reaching as great a degree as when, in the ordinary course of events, the bladder slowly fills with urine from the upper urinary tract. That actual muscular contraction must have taken place as the result of filling is demonstrated by the fact that the pressure subsides gradually if the volume is allowed to remain constant. The observations of Holmes[5] demonstrated this point very clearly.

Denny-Brown and Graeme Robertson[3] have shown that a contraction of the detrusor muscle may also be initiated by a momentary pressure applied to the bladder through the abdominal wall. Not only so, but these workers also recorded the occurrence of spontaneous waves of vesical pressure. These were waves of relatively small amplitude, producing pressure changes of not more than 20 to 25 cm. of water. Such spontaneous waves were observed only in *Case* I of this series, in whom well-marked spontaneous contractions were seen.

The bladder may not apparently exhibit this active and irritable condition in every case. In *Case* 3 the pressure curve did not rise steeply with increasing volume (*see Fig.* 529), and this, as well as the large size of the cystogram made after rapid filling with contrast medium (*see Fig.* 526), reveals no evidence of the resistance to filling so characteristic of the other cases.

2. **Complete Transverse Cord Lesions.**—A very different behaviour of the detrusor muscle was manifest in these cases, following recovery of reflex activity in the distal part of the spinal cord. Observations of the bladder pressure in *Case* 6 revealed a very active condition of that muscle. Sudden and considerable rises of pressure took place at intervals without apparent cause (*see Fig.* 535). This same phenomenon was observed by Holmes.[5]

In *Case* 7 observations on the intravesical pressure revealed similar powerful contractions of the detrusor muscle. These were also demonstrated very effectively by the powerful stream with which the urine was expelled from the bladder. The urinary stream was as forcible and as broad as that of normal micturition, and, quite apart from the fact that the patient was lying at rest without any straining, could only have been produced by strong contraction of the bladder wall.

It is very evident that the existence of active lower spinal segments has a profound influence on the behaviour of the detrusor muscle. In the presence of such active segments detrusor contractions similar to the normal continue to take place.

BEHAVIOUR OF THE SPHINCTER MECHANISM

1. **Lesions of the Conus and Cauda Equina.**—The sphincter mechanism consists of two essential parts, the one composed of smooth muscle and known as the internal sphincter, the other composed of striped muscle. The nature of the lesion leaves no room for doubt as to the behaviour of the latter. Since its innervation from the sacral segments of the spinal cord has been destroyed it must be entirely paralysed.

The evidence of cystography (*see Figs.* 513, 522, 526, 532) and of cystoscopy revealed that in every one of these cases there was wide relaxation of the vesical

orifice, and appeared to demonstrate complete incompetence of the internal sphincter.

The invariable presence of residual urine and the effort required to evacuate urine from the bladder showed that there existed in these cases a considerable resistance to emptying of the bladder. Since the external sphincter was paralysed and the internal sphincter incompetent it was necessary to find some explanation to account for this resistance. The only reasonable explanation seemed to be the existence of a mechanical factor—the pressure and elasticity of the tissues surrounding the urethra in the region of the triangular ligament. Dennig[2] came to a similar conclusion in the case of the dog after destruction of all three nerve pairs. Schwarz[10] also emphasized that the elastic action of the closing muscle is alone sufficient to maintain continence against a certain pressure.

When this work was first reported (Hunterian Lecture, Jan. 31, 1934) it was stated as a result of the above observations that the sphincter mechanism behaved entirely in a passive manner, and that there existed only this mechanical resistance to evacuation of the bladder. Denny-Brown and Graeme Robertson,[3] however, have placed on record observations which suggest that the internal sphincter plays an active part in bladder function in these cases. They state : " During spontaneous vesical activity the internal sphincter reacts by relaxations reciprocal with the intensity of contraction of the detrusor."

It appeared very difficult to reconcile the findings of Denny-Brown and Graeme Robertson with those above mentioned. But it seemed at least possible that the wide relaxation evident in the cystograms resulted from the technique employed, in which the skiagram was made immediately following the sudden injection of contrast medium. The problem was therefore further investigated. At the observations on March 9, 1935, in *Case* 1, a skiagram made at a time when no fluid was passing out of the bladder showed an open bladder neck and a widely dilated posterior urethra (*see Fig.* 516). In another film made three or four minutes after he had passed about 50 c.c. from the bladder no contrast medium can be seen in the posterior urethra (*see Fig.* 517). A second film made on the same occasion as *Fig.* 513 after the evacuation of a good deal of the fluid also showed a closed bladder neck (*see Fig.* 514).

Two important facts were demonstrated : (1) That even when the internal sphincter was widely dilated there was no escape of fluid ; (2) That the internal sphincter does not always remain open.

A further series of observations was made (Sept. 18, 1935) in this case. After the introduction of fluid well-marked contractions of the bladder were evident, on one occasion the pressure increasing from 40 to 65 cm., on another from 38 to 65 cm. A film was made when the pressure had just fallen to 38 cm. following a spontaneous contraction. In this film there is wide relaxation of the vesical orifice and posterior urethra (*see Fig.* 518): 85 c.c. of fluid was then evacuated from the bladder and a film made with the pressure at 16 cm., and another when he attempted to pass urine (at a pressure of 38 cm.). In both these films (*see Fig.* 519) dilatation of the vesical orifice and posterior urethra is evident though very much less in degree than in the first film.

It is important to notice that the widest dilatation of the posterior urethra was present in the interval between the spontaneous vesical contractions. This does not confirm the interpretation given by Denny-Brown and Graeme Robertson[3] of

their observations on discharge into the urethra, according to which the internal sphincter should have been closed in the interval between the vesical contractions. On the other hand, the smaller degree of dilatation of the posterior urethra (seen after some of the fluid had been evacuated from the bladder—*Fig. 519*) was not made greater by the straining efforts to pass urine, although the film was made when the intravesical pressure was 38 cm.—the pressure at which a previous film had revealed the widest dilatation of the posterior urethra. This appears to be strong evidence in favour of the view that the condition of the smooth muscle sphincter is related to that of the detrusor, and that it is not simply a mechanical effect determined by the intravesical pressure.

In *Case* 3 the condition of the sphincter, as well as that of the detrusor, appears to have been different. In this case there was filling of the posterior urethra even when the greater quantity of the fluid had been evacuated (*see Figs.* 526–528). The degree of distension of the posterior urethra diminished as the volume of fluid in the bladder was reduced. The interpretation of this observation must be that the internal sphincter is incompetent and that with decrease of the intravesical pressure the size of the posterior urethra is diminished by the elastic action of the structures which surround it. Thus in this type of case the smooth muscle sphincter, just as the detrusor, becomes completely atonic.

In general it may be concluded from these observations that there is a considerable and purely mechanical resistance to the outflow of the urine from the bladder which must be attributed to the elasticity of the tissues in the region of the triangular ligament. There may be also closure at the vesical orifice itself, and the findings recorded here support the view of a reciprocal relationship between the detrusor muscle and the internal sphincter (Denny-Brown and Graeme Robertson).

2. Complete Transverse Cord Lesions.—The behaviour of the sphincter apparatus in such lesions has been carefully analysed by Denny-Brown and Graeme Robertson.[3] The only available evidence in this work is derived from *Case* 7. In this case the escape of fluid around the catheter during the pressure estimations, and the broad calibre of the urinary stream, testified to the fact that the urethral sphincters must have undergone a full relaxation in co-ordination with the detrusor contraction.

THE FUNCTION OF THE BLADDER AS A WHOLE

1. Lesions of Conus and Cauda Equina.—The remarkable degree of control which these patients were able to exercise clearly resulted from their ability, by straining efforts of the abdominal muscles, passively to force urine from the bladder. But in spite of the overwhelming importance of the abdominal straining as the expulsive force in urination it is certain that the urination is not entirely a passive procedure. It cannot be doubted that the stimulation to the detrusor muscle which results from the abdominal straining sets up some contraction of that muscle, which assists, if somewhat weakly, the expulsion of the urine. On one occasion in *Case* 1 abdominal straining had proved ineffective, but after pressure applied to the lower abdomen the desire to urinate occurred and further effort was successful. This shows that the activity of the bladder itself may be necessary in addition to the abdominal straining. In this instance it is to be presumed that the stimulation to the bladder wall set up detrusor contraction which in its turn

caused the internal sphincter to relax. Urination was thus facilitated when the patient made further efforts.

In spite of the degree of voluntary control which these patients can achieve, incontinence is a perpetual threat to their comfort. It is not probable that this is simply passive in character, from overflow. The sequence of events would appear to be that distension of the bladder to a certain point leads to sensation of bladder fullness, which is evidently transmitted by the hypogastric nerves. It is not unlikely that at this point a detrusor contraction is actually present, since Denny-Brown and Graeme Robertson's records show that the sensation of discomfort was related to contractions of the detrusor. At this point, too, the internal sphincter is no doubt widely relaxed, as was shown in a cystogram made in *Case* 1, where, although there was well-marked sensation, no fluid was escaping from the bladder (*see Fig.* 516). A little later, possibly as a result of a spontaneous contraction of the detrusor, or from some other cause such as a sudden movement or cough, some urine escapes from the bladder. It is important to notice that the amount of urine which escapes in this way at any one time is small, and in no way to be compared with the massive emptyings which result from deliberate urination. It is, indeed, only because the bladder is of itself so ineffective in expelling urine that the patient can control his urination to the degree described above.

2. Complete Transverse Lesions.—The behaviour of the bladder as a whole is well shown by an observation in *Case* 7 in which the urinary evacuations were watched for some time. Spontaneous evacuation occurred seven times as follows :—

1.	55 c.c.						
2.	95 c.c.	at an interval of	35	minutes after	1		
3.	85 c.c.	,, ,, ,,	,, 16	,,	,,	2	
4.	90 c.c.	,, ,, ,,	,, 10	,,	,,	3	
5.	130 c.c.	,, ,, ,,	,, $7\frac{1}{2}$	,,	,,	4	
6.	130 c.c.	,, ,, ,,	,, $8\frac{1}{2}$	,,	,,	5	
7.	125 c.c.	,, ,, ,,	,, 8	,,	,,	the previous evacuation	

Seven minutes after the last evacuation 100 c.c. of urine was found in the bladder, so that the amount of residual may be reckoned to be very small. Each evacuation seemed to be of normal force and calibre, and no urine escaped in the intervals. The features of this type of urination are, therefore, comparable to normal micturition—a powerful broad stream with almost complete emptying of the bladder. The fundamental difference from normal micturition is the entire absence of voluntary control. Incontinence is, therefore, absolute, and urinary evacuation takes place at intervals in a manner which may truly be described as " periodic reflex micturition " (Thomson-Walker[11]).

Case 7 always had a sensation from his bladder which preceded by a few seconds the actual evacuation and was evidently produced by the commencing activity of the bladder. This must have been transmitted by way of the hypogastric nerves. In spite, however, of the integrity of the latter he was not able to exercise any control over his bladder function.

The reflex facilitation of micturition from stimulations applied to areas below the level of the lesion have been studied by Head and Riddoch[4] and by Denny-Brown and Graeme Robertson.[3] Stimulation of the glans penis was shown to be effective in setting up reflex micturition in *Case* 7 and also in *Case* 8, the latter being, however, an incomplete lesion.

CONCLUSIONS

A study of the cases recorded in this work reveals quite clearly the fundamental importance to bladder function of active sacral spinal segments. The influence of these segments below a complete transverse lesion is such as to promote a perfect reflex micturition, which differs essentially from the normal in its entire independence of voluntary control.

The behaviour of the bladder in lesions of the conus and cauda equina is evidence of a limited degree of function mediated by the peripheral nerve ganglia. It has, however, been shown above that this function is not, of itself, efficient in evacuating urine from the bladder. For even when the internal sphincter is widely relaxed, and the detrusor in contraction, there may be no escape of fluid from the bladder. It can only be concluded, therefore, that its peripheral innervation alone determines a very ineffective bladder function.

It is without doubt the existence of a considerable mechanical resistance in the region of the triangular ligament which deprives this function of the bladder of most of its effect. But it is in virtue of this resistance combined with the patient's ability to expel urine by straining with his abdominal muscles which provides him with the means of living in relative comfort. This patient is, therefore, in much better circumstance than the patient with a transverse cord lesion who, though he has a very perfect reflex micturition, is not able to control it.

The author wishes to express his thanks to Professor Hugh H. Young, of Baltimore, and to Herr Professor E. Rehn, of Freiburg im Breisgau, for their courtesy in permitting him to study the cases under their care. And it is with especial pleasure that he records his great indebtedness to Mr. Geoffrey Jefferson for his continued interest and advice.

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A CASE OF SPINAL TUMOUR

By T. SATAKOPAN and N. MANGESH RAO

DEPARTMENT OF PATHOLOGY, MEDICAL COLLEGE, MADRAS

CHENCHIAH, a Hindu male aged 18 years, a ryot of Nellore district, was admitted to the General Hospital, Madras (under T. S.) on June 16, 1934, for inability to walk and pains in the back and sides of the chest of a year's duration.

HISTORY.—Nothing of clinical importance was noted. Prior to the present complaint, the patient was in perfect health, doing daily labour in the paddy fields. He is a teetotaller and never had any venereal infection.

About a year ago the patient noticed that he was progressively getting weaker in his legs. About two months later he could not stand without help and felt that the legs were giving way under him. At this time he suffered from sharp attacks of pain in the middle of his back and radiating to both sides of his chest. The weakness in the lower limbs steadily progressed, and in the last three months prior to admission he was unable to stand up even with assistance. Later any attempt to move the legs resulted in involuntary contractions. Sometimes this occurred spontaneously. A month ago he had retention of urine and fæces. He was catheterized in a hospital and later sent to the General Hospital.

ON ADMISSION.—The patient was rather poorly nourished, slightly anæmic, and had moderate pyorrhœa. Cardiovascular, respiratory, and alimentary systems were normal. No abnormal changes were seen in blood, urine, or motion.

Neurological Examination (T. S.).—Mental powers were normal and unimpaired. Both ocular fundi were normal. No abnormal changes were seen above the chest.

Musculature.—Lower limbs : Some wasting of muscles with occasional flexor spasms was seen. Motor power was considerably diminished in both limbs, the weakness being more marked in the left. Both legs were very spastic. The muscles of the face, neck, upper limbs, and trunk were normal.

Sensory.—Sensations in the lower limbs were moderately diminished. The loss of proprioceptive sensations was more marked than the others in the left leg, but thermal and pain sensations were diminished more in the right leg. Appreciation of light touch was impaired on the trunk up to the 8th dorsal segment on the right and 10th dorsal segment on the left. Girdle pains were present corresponding to the 10th dorsal segment, i.e., on a level with the 7th–8th dorsal vertebræ.

Reflexes.—These were as follows :—

	RIGHT LOWER LIMB	LEFT LOWER LIMB
Babinski	+	+
Cremasteric	—	—
Abdominal, lower	—	—
Abdominal, upper	±	=
Knee-jerks	+ +	+ ± +
Ankle	+ +	+ + +
Patellar and ankle clonus	+	+ +

Organic reflexes : Bouts of obstinate constipation and retention of urine occurred.

Electrical Reactions.—No reaction of degeneration was noted in the muscles of lower limbs.

Other Investigations.—Roentgenogram of vertebral column was negative. Wassermann and Kahn reactions were negative.

Lumbar Puncture.—Fluid was under pressure, pale yellow but clear. Delayed spontaneous coagulation occurred. Total proteins, 890 mgrm. per cent; albumin, 554·6 mgrm. per cent; globulin, 325·4 mgrm. per cent; lymphocytes, 3 per c.c. Gold curve and Wassermann reaction of fluid were negative. Clearly it was a case of Froin's syndrome.

FIG 541 —Antero-posterior view of spinal column after injection of lipiodol.

On July 24 a cisterna puncture and injection of lipiodol was done by N. M. R. and on July 27 a lumbar puncture and injection of 1 c.c. of lipiodol (heavy) in high Trendelenburg position was done and roentgenograms were taken (*Fig.* 541). They showed a definite block opposite the 7th dorsal vertebra. The case was transferred to the surgical side under N. M. R.

OPERATION (Oct. 16, by N. M. R.).—Incision from the 3rd to 10th dorsal spines was made, the spines were exposed and removed from the 5th to 9th inclusive. The laminæ of the 7th and 8th dorsal vertebræ were trephined and the edges were nibbled away. The dura was exposed and lifted by sharp hooks followed by catgut sutures. The dura was incised for about 2½ in. in the middle line, exposing an œdematous arachnoid with a small yellow calcareous-like nodule at the lower part. There was no visible pulsation. In the lower part of the wound

the pale yellow-coloured cord could be seen.   The arachnoid was incised carefully in the upper part, exposing a vascular tumour.   This was slowly shelled out.   It occupied the left dorso-lateral position in the theca and extended slightly to the right across the mid-line.   The tumour was not attached to the dura but was entirely in the arachnoid tissue.   After this the cerebrospinal fluid with some lipiodol escaped from above and visible pulsation became evident.

After the usual toilet the theca was closed with fine silk and the wound closed in layers.   The patient was nursed in the prone position and put on hexamine and injections of cylotropine.   Except for a small irregular rise in temperature his

FIG 542 —Roentgenogram after the operation showing most of the lipiodol at the bottom of the theca

condition was good and the wound healed by first intention.   He began to improve, and by Nov. 28 he was able to move about without aid.   On Nov. 12 a lumbar puncture showed 300 mm. pressure, and 20 c.c. of fluid were withdrawn.   The cerebrospinal fluid showed 32 mgrm. per cent of albumin and a trace of globulin; the cell count was about normal.   On Nov. 19 another lumbar puncture showed 240 mm. pressure, and 20 c.c. were withdrawn.   After this his progress was steady.   *Fig.* 542 shows the spinal condition after operation.

REPORTS OF EXAMINATION (T. S.).—

Nov. 10, 1934.—Increased strength in legs ; flexor spasms and root pains absent.

Nov. 28, 1934.—Patient is able to walk about without aid ; gait still slightly spastic ; Rombergism is greatly diminished.   Sensory changes and signs of damage to pyramidal tract persist.

Feb. 1, 1935.—General nutrition is very good. The patient is able to walk about very freely with just a trace of stiffness. Light touch and kinæsthetic sensibility are not completely recovered. Rombergism and root pains are absent. In so far as the damage to the pyramidal tract is concerned the deep jerks are still a little 'gay' on both sides and the superficial skin reflexes are still absent. This is probably due to some permanent damage caused by the tumour.

FIG. 543 — Painting of a vascular fibroma weighing 45 gr. Site: dorso-left-lateral position over the 8-9th thoracic segments, in the arachnoid, but not attached to the dura. (× 2.)
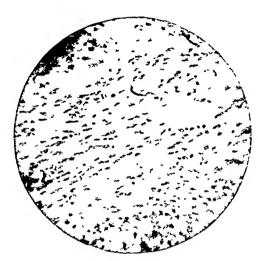
FIG. 544 —High-power photomicrograph of section of tumour.

The patient is able to run and turn sharply round without stumbling and appears normal except for the slightly exaggerated tendon reflexes in the legs and absence of skin reflexes.

He was discharged quite happy and pleased on March 17, 1935.

The tumour was fairly vascular and weighed 45 gr.

PATHOLOGICAL REPORT.—Cellular fibroma which is very vascular; areas of hæmorrhage are also seen. (*Figs.* 543, 544.)

A CARCINOID TUMOUR OF THE LOWER ILEUM

BY W. QUARRY WOOD, EDINBURGH

CARCINOID tumours of the gastro-intestinal tract have excited a great deal of interest among pathologists during the past twenty years, an interest which is perhaps out of proportion to their clinical importance. They are rare tumours, but in their origin, structure, and method of spread they present peculiarities which are responsible for the amount of attention they have attracted. They are most common in the appendix, but have been recorded as occurring in all parts of the abdominal alimentary canal. The cases recorded in the small intestine up to the latter part of 1934 numbered 152; since then a few additional cases have appeared in the literature. The comparative rarity of the tumour and the fact that it is now being recognized that a rather characteristic group of symptoms are frequently associated with the condition may justify the publication of another case.
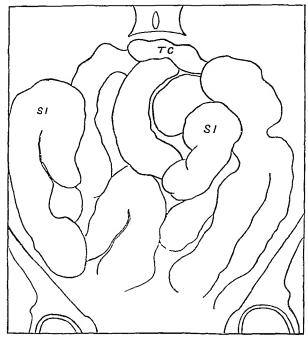
FIG 545 —A tracing of the X-ray photograph showing distended coils of small intestine (S I)
A small amount of barium has entered the transverse colon (T C)

CASE REPORT

A woman, aged 62, had an attack of abdominal pain and flatulent distension in the spring of 1933, a year before operation She was free from symptoms during the summer, but in the late autumn attacks of pain and flatulence recurred. In the beginning of January, 1934, the attacks became more severe and she was much troubled with constipation She lost a stone in weight during the last few months before operation. Her symptoms suggested

chronic intestinal obstruction probably due to a carcinoma of the colon. X-ray examination, however, showed that the site of the obstruction was at the lower end of the small intestine (*Fig. 545*). On March 18 the abdomen was opened through a right paramedian incision and a tumour was found at the ileocæcal junction. This was regarded as a carcinoma. The small intestine was much distended and an immediate resection was considered to be unsafe. The ileum was accordingly divided about 6 in. above the ileocæcal junction, and the proximal
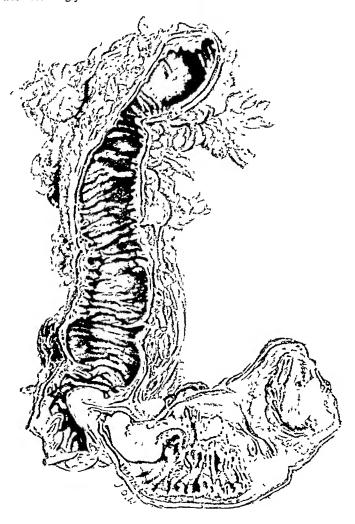
FIG. 546.—The appearance of the tumour on section.

end united to the transverse colon by a lateral anastomosis. On April 15 resection of the terminal ileum, cæcum, and ascending colon was carried out. The patient made a good recovery from the operation and when seen on Nov. 24, 1935, was found to be in excellent health.

The appearance of the specimen is well shown in *Fig. 546*. The cut surface of the tumour presents a yellowish colour which was very striking in the fresh condition. It is seen to be growing from the upper border of the terminal part of the ileum about 2 cm. proximal to the ileocæcal valve. It forms a flattened cake in the position of the mucous,

submucous, and muscular coats, and has become buckled on itself owing to contraction of its basal part. This has caused it to form a rounded projection which is obstructing the lumen of the bowel The tumour tissue can be seen to extend through the muscularis. The ileum proximal to the growth shows a well-marked degree of hypertrophy and dilatation. The bowel distal to the tumour is normal in appearance except that the ileocæcal valve is unduly prominent. The orifice of the appendix is occupied by a probe. The appendix is normal in appearance, showing no evidence of either inflammation or tumour.
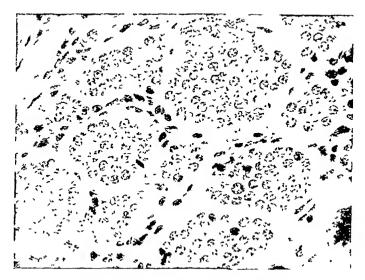
FIG. 547 —The microscopical appearance of the tumour.

The microscopical appearance of the tumour is seen in *Fig.* 547. A report by Colonel W. F. Harvey states : " The condition is a typical carcinoid tumour of spheroidal-cell type It presents solid alveolar masses of a uniform-cell type, situated in the submucosa, the muscularis, and in the subserosa. The tumour growth in this case is much more extensive than those one has seen." One lymphatic gland was found about 2·5 cm. above the growth ; it was the seat of a metastatic deposit. A small nodule of doubtful nature was found in the mesentery adjacent to the tumour ; this consisted of tumour tissue, but it was uncertain whether it represented an infected lymphatic gland or not.

DISCUSSION

The most striking features of the carcinoid tumour are the yellowish colour of the cut surface on naked-eye examination and the presence on microscopical examination of silver-reducing granules in the cytoplasm. The cells of the tumour are frequently arranged in solid columns, resembling certain types of basal-cell carcinoma. The histogenesis of the tumour has aroused much speculation. Argentaffine cells, the so-called Kultschitsky cells, are normally present in the crypts of Lieberkühn ; they are concentrated at the bases of the crypts, being pear-shaped with broad bases lying on the basement membrane and with narrow bottle-shaped necks leading up to the lumen of the crypt. The cytoplasm appears lighter after staining than that of the neighbouring cells. They are found in all parts of the intestinal tract but are most numerous in the appendix and terminal ileum.

Their origin is uncertain. Raiford[1] suggests that they are probably of ectodermal origin and have migrated early from the neural crest tò form a specialized part of the chromaffin system. The affinity for silver and the similarity to the cells of the adrenal which they present are in favour of this view. Most pathologists have followed Masson[2] in attributing the origin of carcinoid tumours to these cells. Raiford makes the following statement: " It is ascertained, beyond reasonable doubt, that the carcinoid tumours arise from the cells of Kultschitsky or the chromo-argentaffine cells of Masson and that these cells are normally present in the intestinal tract of man. They are thought to be chromaffin in nature and the tumours are consequently chromaffin tumours. Their significance, or the stimulus resulting in tumour formation, can at best remain a matter of speculation." Masson also demonstrated a peculiar relationship between carcinoid cells and nerve-fibres, said to resemble the relationship between nerve-fibres and nævus cells. The carcinoids were first described and separated from the carcinomas by Obendorfer[3] in 1907.

From the clinical point of view, most interest lies in the nature of the symptoms which are associated with the tumour and in its degree of malignancy. In carcinoid tumours of the appendix metastasis to the regional lymphatic glands is extremely rare and distant metastasis is practically unknown. In the small intestine the tumours are much more malignant, secondary growths having been frequently met with in the regional lymphatic glands and occasionally in the liver, the lungs, and other organs. A survey of several of the recently recorded cases of carcinoid tumour of the small intestine shows that a characteristic group of symptoms may sometimes be present and that a pre-operative diagnosis of the probability of the lesion being a carcinoid might be possible. A brief reference to a few of the recent cases is of interest. The case reported by Christopher[4] occurred in a woman of 55. The tumour was situated 8 in. proximal to the ileocæcal junction. It had caused recurrent attacks of abdominal pain over a period of three years with a mild degree of intestinal obstruction. A local resection of the affected piece of bowel was followed by recovery. No metastases were found in the regional lymphatic glands. Two cases reported by Lee and Taylor[5] resemble my own case very closely. In one, a woman aged 51, attacks of abdominal pain associated with loss of weight and constipation had occurred over a period of thirteen months. A tumour was found at the ileocæcal junction, and resection of the terminal part of the ileum, the cæcum, and the ascending colon was performed. The tumour had extended through the muscular coat of the bowel and one lymph gland was almost entirely replaced by a metastatic growth. This patient was free from abdominal symptoms twenty-three months later. The second case was also in a woman, who was 53 years of age. Similar symptoms had been present, but only for a period of one month. The tumour in this case was 10 cm. proximal to the ileocæcal valve and a similar operation was carried out. This tumour had also spread through the muscularis and had infected one of the neighbouring lymphatic glands. The patient was well twenty-two months later. It is of interest that these three patients and my own were females of about the same age.

The clinical result of a carcinoid tumour of the small intestine is likely to be a slowly progressing stenosis of the bowel. This is borne out by a consideration of the above cases and by a survey of the literature. In a patient after middle age presenting symptoms of chronic intestinal obstruction, where the radiological

examination shows the site of the lesion to be the lower part of the small intestine, the possibility of its being a carcinoid tumour should be considered. An adeno-carcinoma will present similar symptoms and it will generally be impossible to differentiate between the two until the tumour has been sectioned. The distinction is of some importance in view of the lesser degree of malignancy of the carcinoid. In the past, however, an unjustifiably optimistic view seems to have been held in regard to the essential nature of these tumours, probably owing to the fact that in the appendix the carcinoid is almost invariably benign. The probability is that all carcinoids are potentially malignant. In the appendix the lesion produces symptoms at an early stage before infiltration has progressed very far. It is to be noted in this connection that the age incidence in carcinoid of the appendix is much lower than in carcinoid of the intestine; in the appendix the average age has been under 30 in several series of cases, while in the small intestine it is between 50 and 60. In the small intestine the tumour reaches a larger size before it gives rise to symptoms, and in these larger tumours infiltration of the muscularis and the serosa are not infrequently present; metastases in the regional lymphatic glands and occasionally in the liver, the lungs, and other organs are sometimes met with. Malignancy seems to be largely a question of the age of the tumour. In the 152 cases collected by Humphreys[6] at the end of 1934, metastases were present in 24·4 per cent. With the addition of 3 out of the 4 cases mentioned in this article the frequency of metastases becomes 25·9 per cent. It is significant that metastases have been found more frequently in the recent cases than in those reported earlier. As compared with adenocarcinoma, the carcinoid tumour is less malignant, but the difference is not so great as has been commonly supposed. The frequency of metastasis in adenocarcinoma of the small intestine is given as 38 per cent by Schleips[7] and as 36 per cent by Craig.[8] It is obvious that the treatment of a carcinoid tumour of the intestine must be a radical operation on the same lines as in adenocarcinoma.

Reference must be made to a further feature of carcinoid tumours. In cases discovered at post-mortem examination the tumours have been found to be multiple in a considerable proportion of cases—probably about a third. In these multiple cases many of the nodules have been of small size and at the ' benign ' stage. It will very seldom be possible to recognize or to deal with such multiple growths in the living subject.

I wish to express my indebtedness to my wife for the coloured illustration of the tumour, to Colonel W. F. Harvey for his help in the preparation of this paper, and to Mr. Hamilton for the photomicrograph of the growth.

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COLLOID TUMOUR OF THE URACHUS INVADING THE BLADDER

BY R. CAMPBELL BEGG, WELLINGTON, NEW ZEALAND

IN 1931 I published in this JOURNAL a case of colloid adenocarcinoma of the urachus invading the bladder vault, and expressed the opinion that the seventeen cases reported in the literature up to that time in no way represented the frequency of the disease. I am now able to report a second case of a similar nature.

W. J., male, aged 54 (Wellington Hospital Case No. 34/5985) was admitted on March 19, 1934, complaining of passing blood in the urine.

HISTORY.—The patient said that two years previously he had received a violent blow in the back and two months thereafter passed a large quantity of blood in his water. The bleeding was apparently profuse and accompanied by clots. Ever since then at intervals of about seven weeks he had had recurrent attacks of a similar nature. These usually lasted about two weeks, but in the intervals, and especially in the few months before admission, he had passed globular masses of a material resembling apple jelly. While during the attacks he was annoyed with frequency, especially at night, and occasional pain on passing clots, he had no symptoms whatever in the intervals. There was nothing of importance in his previous history.

ON EXAMINATION.—The patient appeared to be a trifle anæmic, but the general examination disclosed no physical anomaly. Neither kidney was enlarged,

FIG. 548.—Cystoscopic appearance of bladder invasion by colloid adenocarcinoma of the urachus. The reddish neoplasm is seen shining through a mass of translucent jelly at the bladder apex. The surrounding mucosa is normal.

palpable, or tender. There was slight tenderness on deep pressure in the suprapubic region. The prostate was normal to rectal touch and no induration was felt at the base of the bladder. The Wassermann reaction was negative. The urine contained much mucin, many blood and large epithelial cells, and a few hyaline casts.

Cystoscopy.—The bladder and ureteric orifices were normal with the exception that adherent jelly-like masses were present in the bladder vault somewhat obscuring the view. It was seen, however, that these masses of jelly adhered to a projecting and nodular tumour, the circumference of the base of the growth being about equal to that of a penny (Fig. 548).

A diagnosis was made of colloid adenocarcinoma of the urachus invading the bladder apex; operation was advised but declined, the patient being discharged. He was readmitted for operation on Jan. 20, 1935; this was performed on Jan. 22.

OPERATION.—The radical operation advocated as the result of recurrence in the transversalis-peritoneal space in my previous case was carried out—namely, the removal of the umbilicus and the surrounding skin, a wedge-shaped area of peritoneum and transversalis fascia, and the upper half of the bladder.

An incision was made for $\frac{3}{4}$ in. around the umbilicus and deepened above and at the sides until the peritoneal cavity was opened. The incision was continued in the middle line as far as the symphysis pubis, and the aponeurosis of the recti muscles incised and the muscles retracted. An incision was then made through the peritoneum and transversalis fascia on each side as far out as the course of the obliterated umbilical arteries. The umbilicus was held upwards and forwards and the peritoneo-transversalis flap turned forwards until the posterior surface of the bladder came into view. Without making any inspection of the growth the posterior wall of the bladder was cut transversely with the endothermy knife and with *some separation of the tissue laterally wide* of the bladder, the incision was carried round the organ, removing the upper half of it together with the fat and fasciæ on its superior surface. Some masses of colloid material lying loose in the remaining part of the bladder were removed and the walls brought together leaving a small suprapubic Malecot catheter for drainage. The peritoneum was mobilized, the edges brought together, and the aponeurosis and skin sewn. Following this somewhat extensive operation three was a considerable amount of post-operative distension which was overcome with the use of acetylcholine.

FIG 549 —Sagittal section of the urachus and the bladder apex The whitish tumour is seen to invade the urachus uniformly without infiltrating the surrounding tissues It passes cleanly through the bladder musculature without invading it   The recurved striated appearance of the lower end is apparent

SUBSEQUENT PROGRESS.—The patient made a good recovery and was discharged on Feb. 2. At that time, with the exception of slight frequency due to the diminished size of the bladder, he had no trouble in micturition and the urine was clear. He reported again in June, five months later. Micturition had become normal and there was no evidence of recurrence in the bladder or elsewhere.

PATHOLOGY.—The specimen consisted of the umbilicus and surrounding skin, a wedge of the peritoneum and transversalis fascia, and the upper half of the bladder with the surrounding fat and fascia. Viewed from below the projecting nodular tumour with a mass of colloid the size of a golf ball was seen. The mass was cut sagittally and it was found that the growth occupied the urachus and extended as a cord, following this organ down in its intramural course through the bladder, spreading out in a fan-shaped manner on the vesical mucosa (*Fig.* 549).

Sections of the urachus above the bladder level showed that the whole of the urachal epithelium had been converted into tumour but without invasion of the fascio-muscular wall (*Figs. 550, 551*).

The growth itself at no point showed a tendency to invasion and was of a papillomatous nature rather than acinar. Papillæ with definite cores were seen, but instead of being covered with transitional many-layered epithelium the cells were tall columnar in type with basal nuclei and many goblet cells with a copious secretion of mucin between the papillæ. They were close set and resembled intestinal villi. In spite of the absence of invasion of the cells this growth must be classed as colloid carcinoma, though the term ' adenocarcinoma ' would not apply on account of the absence of acini, and the papilliform nature of it was most unusual for a colloid growth. Abnormal types of growth which can indeed pass from one type into the other are, however, to be expected in this neighbourhood,
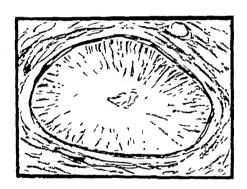
FIG 550—Lens view of section of the urachus 1 cm above the bladder The delicate papillomatous-like fronds have replaced the normal urachal epithe-lium, but the urachus has retained its normal oval appearance A small core of colloid material lies in the centre of the lumen. (⁄ 5)
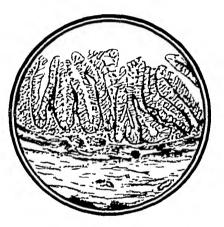
FIG 551—Low-power microscopic view of a small portion of the wall of the urachus It can be seen that each papilliform structure consists of a fibrous-tissue core bearing a blood-vessel The epithelium, however, is of the long columnar type with basal nuclei Many of them are goblet cells full of mucin The strong resem-blance to a section of intestinal mucosa is striking

the epithelial debris and its cells being more or less totipotent in character—the general tendency being towards intestinal forms.

The question of the origin of these colloid tumours and the necessity for being aware of their occurrence and appearance as apical bladder growths was so fully discussed in the previous article that there is little to add. Their rarity, it is true, makes their study of somewhat academic interest, and yet two have occurred in my own practice in the course of ten years, both from the comparatively small city of Wellington. To attain even a probability of cure the treatment must differ from the usual one of resection of the bladder. The symptom of hæmaturia com-bined with the passing of much jelly-like mucus in the urine is almost pathogno-monic, though I have encountered one case of colloid carcinoma of the base of the bladder, the more interesting because it was accompanied by pseudomyxoma peritonei. Faced with such symptoms a primary growth of the urachus may be postulated, and the only appropriate procedure is the radical operation

recommended in the previous paper and carried out in the case now described. The danger of recurrence is not in the bladder but in the space between the transversalis fascia and the peritoneum between the apex of the bladder and the umbilicus.

For the coloured illustrations I am indebted to Dr. P. A. Treahy, Assistant Urologist in the Wellington Hospital Service.

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TWO CASES ILLUSTRATING THE LATENCY OF LARGE RENAL CALCULI AND THEIR RELATION TO PREGNANCY

By JAMES COOK
BIRKENHEAD MUNICIPAL HOSPITAL

THE extreme latency of some urinary calculi is illustrated by the two following cases. In one a perinephric abscess occurring during the puerperium of an eighth pregnancy gave the first hint of serious renal dysfunction; in the other impaction of a small stone in the pelvic outlet was associated with threatened anuria and brought to notice a most interesting collection of stones in the opposite kidney and ureter, the existence of which had not been previously suspected.

Case 1.—Mrs. K. S., aged 36 years, was admitted to Birkenhead Municipal Hospital on July 1, 1935, with a diagnosis of renal neoplasm. Six weeks prior to
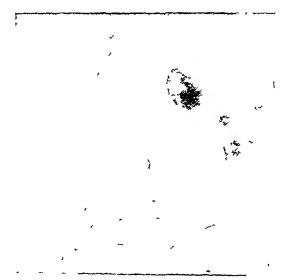
FIG. 552—*Case* 1. X-ray appearances.

admission she had been delivered of her eighth child. Apart from loss of weight and anorexia dating back some ten months, the patient had been entirely symptomless. A slight albuminuria had complicated the last pregnancy. A stone had been removed from the left kidney in 1915. On June 28 a dragging pain was experienced radiating from the left loin to the pubis. There was no frequency or dysuria.

ON EXAMINATION.—A large slightly mobile mass was found occupying the left kidney region. This mass was irregularly nodular and considerable pain was experienced on bimanual examination. The temperature was 100·8° and the pulse 130. The urine was acid and contained albumin, blood, and pus. The specific

gravity was 1020. The blood-urea was 43 mgrm. per 100 c.c. and the blood N.P.N. 40 mgrm. per 100 per c.c.

The diagnosis of a large branched phosphatic stone was made, and the presence of this stone was confirmed by X-ray examination (*Fig.* 552). In view of the clinical findings, a left-sided pyonephrosis was considered a probable complication of the stone.

OPERATION (July 8).—The left kidney was exposed through the usual lumbar incision. It was adherent, especially posteriorly along the line of the previous incision, and there were marked fibro-fatty changes in the perinephric fat. A small perinephric abscess was found in relation to the lower pole of the kidney, but there was no obvious communication with the kidney, the spread of infection being presumably a lymphatic one. There was a marked pyonephrosis. Nephrectomy was performed and on completion of the operation a pint of compatible blood was transfused. A rubber tissue drain was inserted.

Recovery was uninterrupted, blood and pus disappearing from the urine after two days and albumin five days later.

The chief interest in this case is the post-partum flare-up of the renal infection and the fact that such infection did not occur until the eighth pregnancy, or rather that not until a perinephric abscess (one of the rarer complications of renal stone) formed, did the patient's symptoms call for serious investigation.

Case 2.—Mrs. L. D. aged 42 years, was admitted to Birkenhead Municipal Hospital on Aug. 19, 1935, in a state of threatened anuria. The history given was that since August, 1934, a severe right-sided renal colic had recurred at monthly intervals. On Aug. 15, 1935, urinary frequency preceded an attack of right-sided colic, and since then only a few ounces of urine had been passed daily. The patient would admit to only one attack of left-sided renal pain, which was experienced on the day prior to admission to hospital. In June, 1931, while recovering from a left-sided hemiplegia she was delivered of her sixth child. Apart from these six full-term confinements she had had two miscarriages. Her last menstrual period occurred on July 20, 1935.

ON EXAMINATION.—There was marked tenderness on bimanual palpation of the right kidney with cutaneous hyperæsthesia over the line of the right ureter. An indefinite mass was palpable in the left iliac fossa. The urine, which was very scanty, contained albumin, blood, and pus, and gave a culture of *B. coli*. The blood-urea was returned at 117 mgrm. per 100 c.c. and the blood N.P.N. at 85 mgrm. per 100 c.c.

X-ray examination after the administration of uroselectan B showed stones in the left kidney and a large stone in the left ureter (*Fig.* 553). The left kidney appeared very large and hydronephrotic. The right kidney excreted a little uroselectan, but none of it appeared in the ureter, which was jammed by a single stone. The right kidney function appeared to be poor.

FIRST OPERATION (Aug. 22).—A right-sided pyelotomy was performed and the stone removed. The kidney was hydronephrotic. The incision in the pelvis was not sutured, but a rubber drainage tube was passed down to the opening.

Thereafter the patient's general condition rapidly improved and there was a free excretion of urine. On Aug. 23 the blood-urea was 61 mgrm. per 100 c.c. and the N.P.N. 58 mgrm. per 100 c.c. On Sept. 2 the blood-urea was 44 mgrm.

per 100 c.c. and the N.P.N. 42 mgrm. per 100 c.c. By Sept. 6 the renal function had ceased to cause anxiety, but on the evening of that day the patient had an incomplete abortion which was completed at 7.30 a.m. on Sept. 7. Her condition was once more critical, but she responded well to a transfusion of compatible blood, and was discharged from hospital on Sept. 23 in good health.

She returned to hospital on Oct. 23. The urine contained some albumin and many leucocytes and gave a culture of coliform bacilli. The blood-urea was 35 mgrm. per 100 c.c. and N.P.N. 45 mgrm. per 100 c.c.

SECOND OPERATION (Oct. 28).—Under percain anæsthesia the left kidney and greater part of the left ureter were removed through a lumbar incision carried
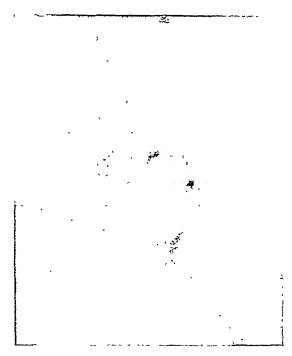
FIG. 553.—*Case 2.* X-ray appearances.

forward parallel to the crest of the ilium. The ureter was mobilized with comparative ease and the only real difficulty encountered during the operation was due to a somewhat thickened renal pedicle. Convalescence was uneventful.

The ureteric stone weighed approximately 50 grm. The length along the curved axis was 5 in., net length $4\frac{1}{8}$ in., and the maximum circumference, near the lower end, was 4 in. The circumference of the stone in the left kidney was approximately $\frac{3}{4}$ in.

Section of the kidney showed some cloudy swelling and loss of cell outline, with a few patches of round-celled infiltration.

THREE CASES OF DUODENAL DIVERTICULUM REMOVED BY OPERATION

By H. N. FLETCHER,

SURGEON, ROYAL SUSSEX COUNTY HOSPITAL, BRIGHTON

and L. I. M. CASTLEDEN,

MEDICAL REGISTRAR, ROYAL SUSSEX COUNTY HOSPITAL, BRIGHTON

Two kinds of diverticula are found in the duodenum : (1) Primary ; (2) Secondary. The latter are due to traction of some neighbouring inflammatory process such as an ulcer, and invariably occur in the first part of the duodenum. They are somewhat rare. The primary diverticula, with which we are now concerned, are much more common. They never arise in the first portion, are seen occasionally in the third and fourth portions, but in the large majority of instances (75 per cent) are found springing from the concave inner aspect of the descending limb, never far from the ampulla of Vater, and lying in close relationship to the head of the pancreas.

Their structure is frail : when dissected out from the areolar tissue which surrounds them they are collapsed, thin-walled, and consist of the mucous and submucous coats of the intestine with perhaps a few muscle fibres gradually fading away as the flask-shaped fundus is reached. Their opening into the bowel varies in size and may be large enough to admit the tip of a finger. There would seem, therefore, to be little hindrance to the entrance and exit of chyme, though the deficiency of muscle fibre in the wall would favour stasis within the sac.

These diverticula are herniæ of the duodenal wall, and the close relationship of their necks to blood-vessels which pierce the concave aspect of the bowel, or to the entry of the common bile-duct, suggests a gradually developing protrusion through a weak spot thus formed. Thus, although occasionally discovered in the young, they are more and more frequently found as age advances. A very full consideration of developmental theories, as indeed of all aspects of the subject, is to be found in Odgers's[1] classical paper and more recently in one by Edwards.[2]

Duodenal diverticula may be solitary or multiple—the former in large preponderance. Their incidence is variously computed by different investigators. Odgers quotes statistics obtained from the post-mortem room, which vary from 3·3 per cent (Linsmayer) to as high as 14·2 and 16 per cent (Baldwin and Grant), and others from X-ray investigations which range from 1·18 per cent (Andrews), 1·2 per cent (Case), 1·5 per cent (McMullan), 3·8 per cent (Spriggs and Marxer), to 5·19 per cent (Cryderman), the five latter giving an average of 2·5 per cent over 11,470 examinations. It is evident, therefore, that as an anatomical entity, duodenal diverticulosis is no rarity. But when we consider its possible clinical importance, we find great differences of opinion.

Rare instances of inflammation or even of perforation of the sac have been recorded, and others of cholangitis or pancreatitis in which the close association of a diverticulum would appear to have been a factor in provoking stasis and inflammation in the respective ducts. Apart, however, from these rarities, the vast

majority of pouches removed by operation or post-mortem, when examined microscopically, show no trace of inflammation past or present, and it is hardly surprising to find scepticism as to whether an uninflamed diverticulum *can* give rise to clinical symptoms. Probably it seldom does. Nevertheless, instances occasionally occur in which it would appear to do so.

Let us take the case of a patient with prolonged and troublesome digestive symptoms conforming to no special type, in whom a duodenal pouch has been found in the course of a bismuth meal and X-ray examination. If other possible causes have been carefully examined, and as far as possible excluded, if medical and dietetic treatment have been tried for a reasonable period without permanent benefit, and particularly if stasis within the pouch has been shown to be present, are we not, under these conditions, justified in regarding it as a causal feature and in recommending an operation? The three cases which we present support such a view. Happily in two, both pure and uncomplicated by other surgical procedure, the relief from symptoms was absolute. One of these has remained well for a year and nine months and the other for eight years. In the third case amelioration was so great as to give the patient the utmost satisfaction, but, as will be seen from the notes given below, it cannot be counted as a pure case, in that a pyloric adhesion was a possible alternative or additional factor in the causation of symptoms.

In no case did the operation itself present any special difficulty, but in this perhaps we were fortunate, for in each instance the neck of the sac was sufficiently distant from the common bile- and pancreatic-duct entrances to give a clear field for removal and suturing, nor were there any adhesions. But it is evident from the descriptions of Odgers[1] and Edwards[2] that in some cases operation may be difficult—e.g., where the pouches are multiple, or adherent—or indeed impossible, as when one or more have developed in direct relationship to the ampulla of Vater.

CASE REPORTS

Case 1.—Mrs. L., aged 64. Admitted to the Royal Sussex County Hospital under H. N. F., on Feb. 8, 1927, complaining of pain in the upper abdomen to the right of the mid-line—five months since onset.

HISTORY.—The pain occurred frequently, in attacks which lasted an hour or more, and which were accompanied by much eructation of wind. She described the pain as a constant, deep ache, severe enough to make her feel faint. It might come on any time and bore no special relation to food. Her appetite was poor and there was always a good deal of gastric flatulence after meals. The bowels were constipated and an action sometimes brought on the pain or made it worse. Micturition was normal. She had lost weight lately.

ON EXAMINATION.—There was nothing special to note in the abdomen except the scar (right paramesial) of an operation for a gangrenous appendix five years previously, and a point tender on pressure one inch to the right of the mid-line, midway between umbilicus and costal margin.

X-ray Examination..—A barium enema revealed no filling defect but caused pain during entry, and there was marked spasm of the transverse colon. A barium meal showed entirely normal behaviour and appearances of the stomach and duodenum, and there was nothing to note in the passage of the meal through the intestine. Barium, however, lodged in a diverticulum, the shadow of which was bounded by the pylorus and the three parts of the duodenum. There was marked tenderness over this pouch on palpation. The position of the stoma could not be identified. Barium remained in it after the rest of the meal had passed through the duodenum.

In view of the protracted pain, discomfort, and loss of weight, it was decided to explore the abdomen.

OPERATION.—Right paramedial incision. Biliary system, pancreas, stomach and duo-denum, right kidney, and colon, all appeared normal. A few minor adhesions in the cæcal region were left undisturbed. There was no sign of a diverticulum on the anterior surface of the duodenum. The latter, after incision of the peritoneum to its right, was mobilized and turned over to the left. The pouch was found bulging through the small arcade of vessels supplying the duodenum on its concave surface and was carefully teased out through a small gap in them, till, with gentle traction on the fundus, a purse-string suture could be placed round the rather wide stoma. The neck was clamped, divided, and ligatured and the circular suture tied. The lateral peritoneum was closed and the abdominal wound sutured.

The position of the stoma was on the postero-inner aspect of the duodenum and appar-ently above the entry of the common bile-duct. The latter was not seen. The pouch was 4 cm. in length, delicate, and thin-walled. Microscopically it showed a mucosal lining with a few muscular fibres thinned out to practically nothing at the fundus. There was no evidence of inflammation, old or recent, in the sac.

SUBSEQUENT PROGRESS.—The patient made a good recovery and was entirely relieved of her pain and flatulence. She has been seen from time to time during the last eight years—on the last occasion, one month ago—and she has kept in excellent health.

Case 2.—Miss M. H., aged 52. Intractable recurrent vomiting for twenty years. Single diverticulum demonstrated by X-rays. Laparotomy. Removal of diverticulum. Complete cure up to one year and nine months after operation.

HISTORY.—Miss M. H. (under care of L. I. M. C.) complained of attacks of intractable vomiting during which everything taken into the stomach was rejected. The sequence of events was that after a period of complete comfort, the patient would experience a feeling of oppression high in the epigastrium and below the right costal margin, acid eructations, bringing up of wind, and slight nausea. Vomiting commenced soon after, and persisted day and night for three or four days in spite of treatment, with special tendency to occur about half an hour after food. In the last three years the syndrome was less related to the taking of food and in addition a favourite time of onset was between 2 and 3 a.m., when she would often vomit food taken eight hours previously. There was no real pain, not more than a feeling of deep epigastric oppression, and no reference to the back or elsewhere. These attacks recurred about every two or three weeks. At the time of her seeking advice they were becoming more frequent and prolonged. She had received much treatment for them, sometimes with apparent relief, and she had gradually eliminated various articles from her diet under the impression that they did not agree with her, until she was now subsisting mainly on toast, dry biscuits, and milk.

Deformity of both hands had been present since birth. The patient had had measles, chicken-pox, scarlet fever, whooping-cough, and ' growing pains ' as a child. There had been no gastro-intestinal trouble until the present vomiting started, and the bowels had always opened regularly and continued to do so between the attacks. No history was obtained of any abnormality in the stools. Micturition was normal. The menopause occurred at 49 without any subjective symptoms. Recently there had been loss of weight. The patient's mother died of carcinoma ventriculi.

ON EXAMINATION.—The patient was a fairly well nourished, rather pale woman of short stature. The tongue was slightly furred but moist, the teeth were very good, and the fauces normal. Her heart was normal in size and situation. A systolic bruit was present at the mitral area conducted towards the axilla, and the pulmonary second sound was accentuated. Blood-pressure 154/84. The lungs were normal, and no abnormality was revealed in the abdomen on physical examination beyond a slightly flabby musculature and slight epigastric tenderness. Eyes and C.N.S. normal. The hands were small, and both showed imperfect development of the thumbs as well as short and atrophic-looking fourth and fifth digits. All the phalanges were present, and there was webbing between the left thumb and index finger. The urine was normal. Hb (Sahli), 87 per cent ; blood-sugar (fasting), 100 mgrm. per 100 c.c.

X-ray Examination.—" The opaque food passed down the œsophagus and entered the stomach in a normal manner. The stomach is fairly normal in position. Tone good, peri-stalsis was normal along both curvatures. Gastric motility normal. There was no direct or indirect evidence of a gastric ulcer. There was no evidence of a permanent filling defect suggestive of a gastric neoplasm. The stomach was empty in two hours. The duodenal ' cap ' was well formed and showed no evidence of spasm or irregularity in outline suggestive

of a duodenal ulcer. In the middle portion of the descending part of the duodenum there was a persistent residue which was present at the end of forty-eight hours. This residue in the erect position appears to have a rounded base with a somewhat flattened upper margin.
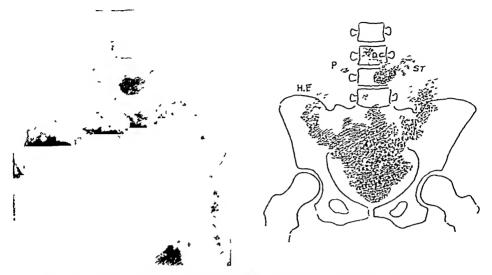
FIG. 554.—*Case 2* Two hours after barium meal. P, Duodenal pouch; DC, Duodenal cap; St, Stomach; HF, Hepatic flexure.
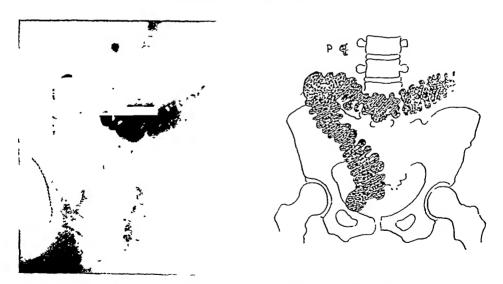
FIG. 555.—*Case 2.* Six hours after barium meal. P, Duodenal pouch.

The rounded base is suggestive of a small diverticulum. There are no indications of any gall-stones that are opaque to X rays. There is no definite evidence of any abnormality in connection with the large or small intestine." (*Figs.* 554–557.)

Fractional Test-meal.—This showed hypochlorhydria of mild degree together with slight delay in secretion, the highest figures for total acidity and free HCl being 35 c.c. and 10 c.c.

N/10 NaOH respectively, which was attained in one and a half hours. The form of both curves was normal.

OPERATION (H. N. F., Feb. 15, 1934).—Right paramesial incision. Stomach irritable with local patchy contractions, otherwise normal. Duodenum more mobile than usual. No
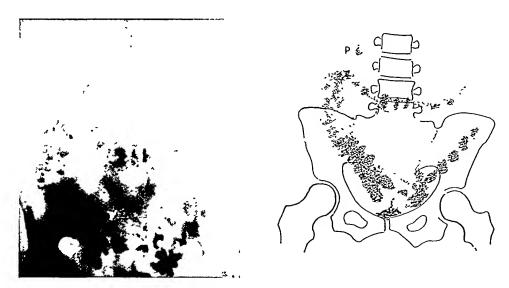
FIG. 556.—*Case* 2. Thirty hours after barium meal. P, Duodenal pouch.
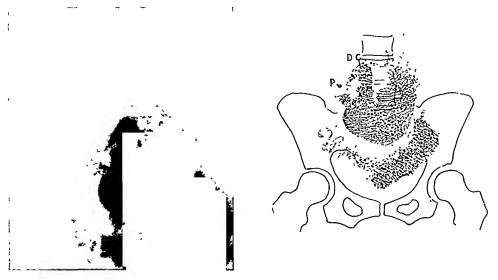
FIG. 557.—*Case* 2. Forty-eight hours after barium meal, with second barium feed just given.
P, Duodenal pouch; DC, Duodenal cap.

outward abnormal appearances.   Gall-bladder, slight subperitoneal deposit of fat; no adhesions or stones.   Liver normal except for superficial fibrosis of capsule opposite rib margin. Ducts and pancreas normal.   Colon, mild ptosis.   Appendix free, no fæcoliths, fibrosis of terminal inch (left *in situ*).   The duodenum was mobilized and turned over to the left.

Immediately the fundus of the diverticulum bulged on its outer side. The pouch, $2\frac{1}{2}$ cm. long, was separated till its neck was defined, arising from the middle of the postero-internal aspect of the second part of the duodenum exactly where the branches of the pancreatico-duodenal arcade enter the bowel wall. Two small vessels, supplying the pouch on its superior and inferior surfaces, were ligatured. The neck of the pouch, $\frac{1}{2}$ cm. in diameter, was divided between clamps, ligatured with catgut, and invaginated by two layers of fine catgut, over which the peritoneal incision was closed.

HISTOLOGY OF POUCH.—" In the sections the structure of the mucosa and submucosa is that of perfectly normal small bowel with abundant villi. Brunner's glands are absent. A few muscle fibres are present. There is no trace of inflammatory infiltration."

SUBSEQUENT PROGRESS.—The patient's convalescence from the operation was uneventful, and during the twenty-one months which have elapsed since then she has had no nausea or vomiting, and has been entirely free from all symptoms. It has been remarkable and most gratifying to see her delight in the re-discovery of the taste of foods " she dared not eat for years." " She no longer has to think about her diet but can eat anything ", and has gained weight.

Case 3.—Miss D. E., aged 42, engaged in the Educational Department of the Sudan Government, consulted one of us (H. N. F.) when home on leave in July, 1929.

HISTORY.—For fifteen years she had been subject to bouts of epigastric pain and gastric flatulence which lasted three to four weeks and which had become worse and more frequent in the last two years. There was never complete digestive comfort between the attacks. An attack was usually ushered in by three or four days of diarrhœa, vomiting, and general abdominal distension. Then followed a month or so of deep-seated, gnawing epigastric pain, going through to the back but with no reference to the shoulders or elsewhere. It was pretty constant in intensity throughout the day. Lying down at night did not take it away, but she slept well. On waking she again experienced it. The pain had no definite relationship to food, though sometimes it was easier for half an hour or so after a meal. The quantity and quality of the food taken did not seem to influence the pain much, but she had little appetite and for the most part would confine herself to a light diet or 'slops' during an attack.

Eructation of wind was a marked feature, with some, but incomplete, relief, and hot water and sod. bicarb. helped in so far as they facilitated its expulsion. Nausea was occasionally present and, rarely, vomiting. The latter did not relieve the pain—indeed, it seemed to increase it. The bowels, always constipated, were kept active by ' purgen ' or magnesia. Mucus in small quantity was now and then observed in the stools and there was always a good deal of intestinal flatulence. Menstruation was three-weekly, scanty, and without pain. Micturition was normal.

The previous history, beyond childish ailments and two short attacks of dysentery in the Sudan, revealed nothing important. Her work was strenuous and she had noticed that the attacks were apt to come on when she was overtired. All her teeth had been taken out two years previously, without any apparent benefit.
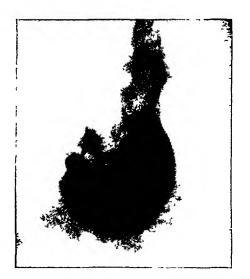
ON EXAMINATION.—When first seen in July, 1929, the patient was having a slight attack. The tongue was clean, her dentures were satisfactory, the tonsils and nasal passages apparently healthy. The thyroid, heart, lungs, and kidneys were all normal. The body was fairly well clothed. There was localized tenderness mid-way between the xiphisternum and umbilicus, no gastric or intestinal distension, and beyond a mobile and palpable right kidney nothing further of note in the abdomen. Per rectum the pelvic organs appeared normal.

X-ray Examination.—A barium meal and X rays showed some hypotonus of the stomach, which did not fully empty for five and a half hours. There was no evidence of ulcer in stomach or duodenum. A diverticulum of the duodenum was apparent in all films after the stomach had emptied, and some barium remained in it for twenty-four hours. Some general visceroptosis was present.

Diagnosis : The patient was of the highly-strung, extremely conscientious type. Though there was evident stasis in the duodenal pouch it seemed doubtful if this was the cause of her symptoms, which were regarded as being probably due to nervous overstrain in a sensitive subject, with, perhaps, a contribution from visceroptosis and constipation. She was therefore advised three weeks rest in bed, sensible feeding up, with bromide and belladonna and cod-liver oil and malt as medicine.

With this she improved and returned soon after to the Sudan.   She was not seen again until her leave in the following summer.   She had kept well for a few months after her rest but then the attacks returned.
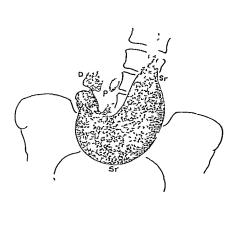
FIG. 558 —*Case* 3.   Just after barium meal.   St, Stomach;   D, Duodenal cap;   P, Pouch.
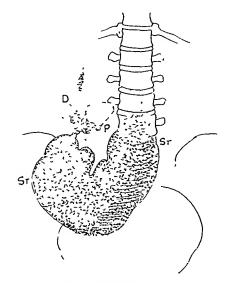
FIG. 559.—*Case* 3.   Quarter of an hour after barium meal.   St, Stomach;
D, Duodenum;   P, Pouch.

A further barium meal was given by Dr. Barrington Prowse in June, 1930, with the following report (*Figs.* 558–563).   " Ptosis and displacement of stomach to the right—hypotonus but no delay in emptying—duodenal ' cap ' in general well-formed but showed variable deficiency and want of tone on the inner side.   In this region a diverticulum soon became evident communicating with the duodenum, though its stoma could not be seen.   The shadow

was roughly triangular with the base downward and to the right, and it lay slightly above and to the inner side of the ' cap '. There was no delay in the duodenum itself, food passed through it normally, but a small quantity of bismuth persisted for many hours in the dependent corner
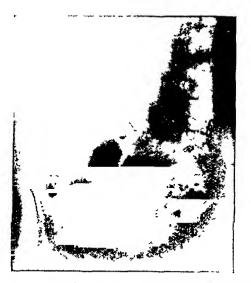
FIG. 560 —*Case* 3. Two hours after barium meal   St, Stomach, P, Pouch.
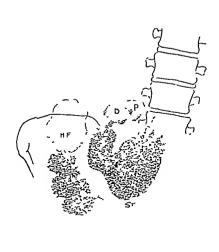
FIG 561 —*Case* 3.   Three and three-quarter hours after barium meal   P, Pouch;
C, Cæcum, I, Ileum.
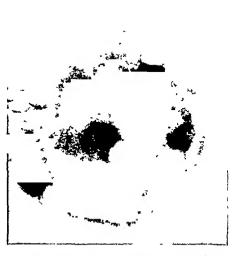
of the pouch. It could, however, be dislodged fairly easily in the supine position." Eight hours after ingestion the whole of the meal was in the colon. Shortly after this a second feed of barium emulsion was given and further observation made. It was found that the pyloric end of the stomach was closely applied to the hepatic flexure of the colon and could not be separated by palpation. There was a definite pressure tenderness in this region. " It seems
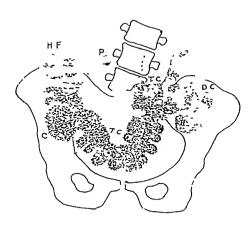
probable that adhesions exist and that they are the cause of the displacement of the stomach to the right and some drag upon the duodenal attachments. What relation they may have to the diverticulum it is difficult to say. There may have been a duodenal or gall-bladder

FIG. 562.—*Case* 3. Half an hour after second barium meal (upright position). St, Stomach; D, Duodenal cap, P, Pouch; HF, Hepatic flexure.

FIG. 563.—*Case* 3. Eight hours after barium meal. P, Pouch; C, Cæcum; HF, Hepatic flexure; TC, Transverse colon; DC, Descending colon.

lesion which has led to adhesions, or the whole thing may be secondary to some abnormality in development."

One felt that in view of this report an exploratory laparotomy was justifiable, but before doing this she was sent to Dr. John Ryle for his opinion. After a helpful analysis of her case, he concurred, and on July 2, 1930, a laparotomy was performed.

OPERATION.—The stomach was normal, no dilatation or hypertrophy. Just below the pylorus a rather well-marked thickening of peritoneum, probably congenital, and constituting a band ½ in. wide, crossed from the tip of the gall-bladder to the inner angle uniting the first and second parts of the duodenum. This, when divided, retracted sharply. There was no sign of gastric or duodenal ulcer. The gall-bladder was thin-walled, and half empty, contained no stones, and showed no signs of previous inflammation. There were no adhesions between the hepatic flexure and the gall-bladder or duodenum as suggested by the X-rays. The appendix looked normal and was left *in situ*. The proximal colon was not unduly mobile and there were no congenital membranes attached to it.

The duodenum was next examined, and anteriorly there were no signs of a diverticulum. It was therefore mobilized by incising the peritoneum on its right, turned over to the left until the small arcade of vessels entering the concave inner border was seen, and the pancreas came into view. Lightly adherent to the latter, flattened, and looking rather like one of its lobes, was the pouch, which was teased out of the connective tissue surrounding it. Its narrow neck, ½ cm. wide, was isolated, the two small vessels supplying it were divided and ligatured, a circular suture of fine catgut was placed around it before clamping, tying, and removing it, the circular suture tied, and a second layer placed over this. The pouch was empty and showed no signs of inflammation. Its neck entered the duodenum about half-way down the second portion, on the postero-medial border, practically in the same plane as the blood-vessels.

The common bile-duct was not seen, but its entrance into the duodenum was certainly below the diverticulum.

Microscopically the wall of the pouch showed muscle fibres at its proximal end, tailing off into mucous membrane and connective tissue at its fundus. There was no evidence of old inflammation, nor were there any Brunner's glands in the mucosa.

SUBSEQUENT PROGRESS.—The patient made an uneventful recovery. She returned to the Sudan in good health at the end of September, 1930. During the next three months the weather was hot and work very strenuous and when she was tired the pain and flatulence came on as before, though much less severely and for a few days only. There was no initial diarrhœa and vomiting, and the pain never went through to the back.

After the New Year 1931 she had a bad attack of cystitis. Since then she has had two minor attacks of the old pain lasting a week or ten days, both when overtired. But apart from these, appetite, digestion, and spirits have been excellent during the four and a half years that have elapsed, and in her own words " she has been an entirely different being".

Comments.—This case has been reported in detail in order that a judgement may be formed whether the marked change in her condition is to be regarded as due to the removal of the diverticulum or whether possibly the division of the band below the pylorus could have any bearing on it. It must be acknowledged that the latter may well have caused the displacement of the stomach to the right (as seen in the second X-ray examination) and possibly the want of tone in the duodenal ' cap '. But to our mind the syndrome of symptoms, particularly the initial diarrhœa and vomiting, described by others as sometimes associated with duodenal diverticula, seem more attributable to the presence of the pouch acting as a reflex source of irritation.

Though her whole health and outlook on life have been profoundly changed for the better, her case cannot be regarded as a ' cure ' in the strict sense of the term.

As so often occurs in reflex disturbances, there would seem to have been two factors at work: (1) A directly determining one; (2) An underlying sensitive nervous system. The former removed, the latter was able to take care of itself, except in times of unusual stress.

SYMPTOMS

From these cases, and from the accounts given of others elsewhere, it would seem difficult to construct any definite syndrome of symptoms diagnostic of duodenal diverticulum when it causes trouble.

Attacks, i.e., periods of especial distress, occur, but there seems seldom to be complete digestive comfort between them, and the history may be a long one.

Pain, of a deep gnawing character, or a heavy discomfort in the epigastric region, is perhaps the most common symptom, and its relationship to food is somewhat vague.

Gastric flatulence and belching of wind, with incomplete relief of pain, was a marked feature in each of our cases.

Vomiting occurred in two cases, and in one it was so incessant as to constitute the outstanding symptom. It was noteworthy that in these two neither belching nor vomiting brought complete relief; indeed in *Case* 3 vomiting made the pain worse.

Diarrhœa always ushered in an attack in *Case* 3, and this symptom has been recorded by other observers.

Tenderness in the region of the diverticulum was present in some degree in all three cases.

As has been suggested, the demonstration of a duodenal diverticulum in a case in which prolonged and somewhat vague symptoms have been present, calls for the most careful search for other possible causes, and only when these have been eliminated, and treatment has failed, should operation be advised.

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FRACTURES OF THE NECK OF THE FEMUR

BY R. WATSON-JONES, LIVERPOOL

PATHOLOGICAL CONSIDERATIONS

FRACTURES of the neck of the femur conform to the same pathological laws as fractures of any other bone. It is now recognized that even in old people there is a free supply of blood to the femoral neck. Every surgeon who has operated on recent fractures has seen the capsule of the joint filled with blood, and the old theory that bone absorption and non-union were due to the inadequate blood-supply has been abandoned. The union of these fractures is governed by the rules of hyperæmic decalcification and ischæmic recalcification.[1, 2] When the fragments are imperfectly immobilized, the trauma of movement gives rise to continued
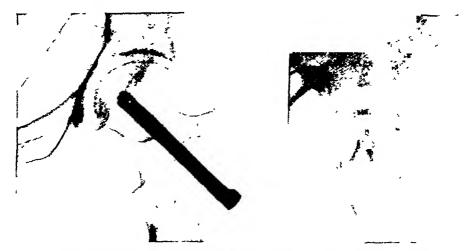
FIG. 564.—High fracture of femoral neck after nailing operation. Antero-posterior and lateral radiographs show that the fracture has firmly united without shortening of the neck.

hyperæmic decalcification. If there is no immobilization at all, this process goes on until the whole of the femoral neck has disappeared. If a plaster spica is used so that the fragments are fixed to some extent but without complete control of rotatory movement, there is a less severe degree of decalcification; nevertheless union is delayed, and if the fracture does unite, there is shortening of the neck. On the other hand, if by operative measures absolute immobility is secured, the fracture unites firmly[3] without decalcification and with minimal shortening of the bone (*Fig.* 564).

Although the fracture is freely supplied with blood, the greater part of this supply is derived from the distal fragment. The bone absorption following hyper-æmic decalcification occurs mainly, therefore, in the distal fragment, and the head

remains practically unchanged. If the fracture is high enough to lie above all capsular attachments, the proximal fragment may be completely avascular, and in such a case there will be radiographic evidence several weeks later. The proximal fragment will retain its original density and will not participate in neighbouring decalcification[1, 4] (*Fig. 565*). The fact that a fracture of the femoral neck may reduce or even cut off the blood-supply of the proximal fragment has three important clinical applications.
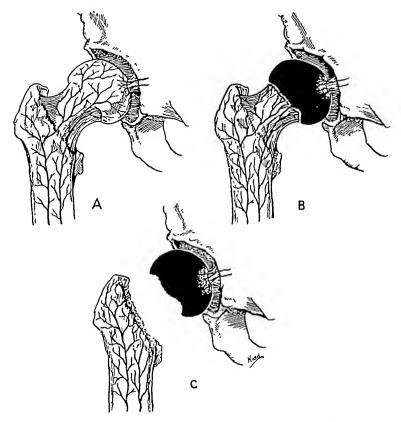
FIG. 565.—Blood-supply after femoral neck fractures. A, The head of the femur is supplied mainly by vessels running up from the neck; B, A subcapital fracture may almost completely deprive the head of its blood-supply; C, If the fracture is not immobilized the vascular neck undergoes hyperæmic decalcification and absorption. The avascular head retains its original density and shows neither decalcification nor absorption.

I. Slow Union of Subcapital Fractures.—In most fractures both the main fragments have an equally free blood-supply and both share in the development of a young connective tissue which will calcify to form callus. If one fragment is avascular, the whole of this new growth must develop from the other fragment, and union is correspondingly delayed. The union of high cervical and subcapital fractures of the femoral neck is therefore slow as compared with basal fractures. But although the vascular supply may account for slow union, it is not a cause of non-union. High fractures of the femoral neck will always unite, but only if immobility is more than usually perfect, and only if *immobilization is continued*

for four to six months or even longer. This is the main reason for the success of the Smith-Petersen nail.[5] For the first time in the history of the treatment of this injury a method has been devised which completely prevents rotatory as well as angulatory movement of the fragments, and which moreover allows immobilization to be continued for six or twelve months without hardship to the patient.

2. The Sequel of Osteo-arthritis.—It is well known that fractures of the neck of the femur are frequently followed by an arthritis of the hip-joint of the degenerative atrophic type (*see Fig. 582*). This arthritis is a sequel to the vascular disturbance which results from a fracture situated above all capsular attachments. The bone of the head of the femur can revascularize and regenerate by the invasion of new blood-vessels from the distal fragment. Articular cartilage is less tolerant, and if it is completely deprived of blood for any length of time it may undergo a degenerative change with resulting arthritis. It is obvious, therefore, that in every high femoral neck fracture absolute immobilization is a matter of urgency, not only to secure union of the fracture, but also to minimize the period during which the blood-supply of the articular cartilage is impaired.

This danger of arthritis of the hip-joint after subcapital fractures suggests that early weight-bearing is inadvisable in these cases. It seems probable that weight-bearing within a few weeks of operation, before the fracture is united and before the cartilage has regained its blood-supply, will increase the tendency to degenerative change.

3. Delayed Treatment and the Treatment of Ununited Fractures.— How long after the fracture has been sustained may the nailing operation still be employed? This depends on the extent to which the proximal fragment has lost its blood-supply, and the degree of decalcification which has occurred in the neck. In low fractures where the femoral head retains an almost normal blood-supply, the nailing operation may be practised many months after fracture, and the only contra-indication to operation is such a degree of absorption and shortening of the femoral neck that good movement is unlikely to be regained. This absorption cannot of course be estimated in the ordinary antero-posterior radiograph because the external rotation deformity gives an appearance of foreshortening of the neck. A lateral radiograph is essential.

On the other hand, the operation is inadvisable after the first six or eight weeks in high fractures where it is probable that the blood-supply of the head is impaired. Where the radiograph proves that the head is completely avascular the procedure is definitely contra-indicated. The degeneration of articular cartilage and osteo-arthritis which may develop even in cases operated on within a few days of injury will be inevitable if revascularization is still further delayed for several weeks or months. Moreover, the bone of the proximal fragment which has been avascular for several months has undergone necrosis and has become too fragile to withstand the pressure of the nail. In one such case a six-months-old subcapital fracture was nailed and the post-operative radiograph showed the nail perfectly placed in the middle of the femoral head. No weight-bearing was permitted and a plaster spica was applied for ten weeks. Nevertheless radiographs at two-monthly intervals showed the nail gradually ploughing its way upwards through the bone, until eight months later it lay in the joint between the head of the femur and the roof of the acetabulum.

Such cases should not be treated by any reconstructive nailing or bone-grafting procedure. They must be accepted as ununited fractures in which arthritis of the hip-joint is inevitable, and dealt with by means of a trochanteric bifurcation osteotomy.

TECHNIQUE OF OPERATION

Although there can be no doubt that a successful nailing operation is a most valuable procedure, an unsuccessful operation is disastrous. There are illustrations in the literature of penetration of the nail through the articular surface into the hip-joint. One such fracture has been seen where a surgeon's operation completely destroyed the articular surfaces and caused fibrous ankylosis. In other cases the nail has missed the proximal fragment altogether. Even apart from such gross misdirection there are other difficulties. In a subcapital fracture the greatest available depth of bone is little more than one inch, the greater part of which must be used if fixation is to be satisfactory. This is only available if the nail enters the head exactly in the middle of its fractured surface (*Fig. 566*). This is of much greater importance than that the axis of the nail should coincide with that of the neck. A nail which is accurately aligned but which lies marginally in the neck is only held in the head by a small sector of bone which may break off during the first few weeks and allow redisplacement of the fragments (*see Fig. 575*).

The Smith-Petersen Operation.—The technique originally described[5] consisted in exposure of the fracture from the front by Smith-Petersen's incision, with a second incision over the trochanter through which the nail was driven. The operation was associated with great difficulties. After a fairly extensive dissection it was still not easy to visualize the axis of the neck, and if the first attempt was unsuccessful it was almost impossible to extract the nail without damaging the bone. The fact that many modifications have been introduced to overcome these difficulties does not detract from, but rather pays tribute to, the genius of the inventor of the nail.

Directing Guides.—The necessity for some mechanical means of directing it became apparent at an early stage. Several types of directing apparatus were made by instrument makers in Liverpool, but all of them were discarded sooner or later because they complicated the technique and were not always reliable. Various forms of guide and aiming apparatus have also been devised by Delbet, Sven Johansson,[6] Lloyd,[7] and Stirling.[8]

Cannulation of the Nail.—The preliminary insertion in the bone of a wire drill in order to guide a cannulated screw was described by Max Richard[9] and by Henschen[10] even before Smith-Petersen described his nail. The application of this principle to the three-flanged nail occurred independently to several surgeons. Sven Johansson,[6] of Gothenburg, and King,[11] of Melbourne, both used centrally cannulated nails and Kirschner wire, and both have developed an extra-articular technique relying on radiographic control. The author's nails[12] were constructed with a wider cannula to take a much heavier guide which would not easily bend or displace, and the technique was applied to the open operation so that radiographic control was not essential. Two types of nail were devised, one with a central cannula and the other cannulated along the margin of one of the blades. If, when the guide had been driven in, it was found to lie centrally in the femoral neck,

a centrally cannulated nail was used; if the guide was found to be eccentric, a laterally cannulated nail was chosen. In practice it was found fairly easy to insert the guide accurately, and the laterally cannulated nail was ultimately discarded.

Stainless Steel Nails.—The first nails produced in England were plated or made of ordinary steel. It was found that these nails gave rise to a severe local
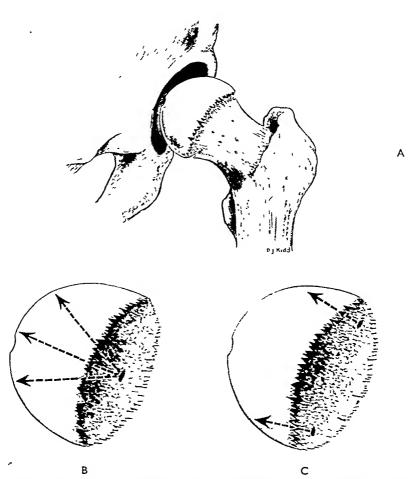
FIG. 566.—A, In a subcapital fracture the greatest available depth of bone may be little more than 1 in.; B, This depth of bone is only available if the nail enters the head exactly in the middle; C, Even if a nail is accurately aligned, if it enters the margin of the head it is only held in position by a thin sector of bone which may break off and allow redisplacement.

reaction with decalcification of the bone and loosening of the nail. When stainless steel was employed this complication did not arise.[3]

Exposure of the Fracture.—Smith-Petersen's anterior incision with a second small incision over the trochanter is associated with all of the difficulties of blind insertion. Apart from confirming the accuracy of reduction, the only value of the extensive dissection lay in recognizing mal-alignment of the nail when it was too

late.   The incision was therefore modified by curving its lower end backwards, raising a flap, and so exposing the femoral neck from the fracture to the trochanter. The operation was very much facilitated, but in one old and feeble patient with impairment of circulation the whole flap sloughed and the patient died after ten weeks.

$\frac{1}{2}$ Sc

FIG. 567 —X-ray measuring rod graduated in quarters of an inch.

A lateral approach is now used, and it is found that through a 6-in. incision the head of the femur, the fracture, the whole length of the femoral neck, and the upper shaft of the femur can be so easily exposed in one field of view that it is a very easy matter to aim accurately.   This change in operative exposure has done as much to facilitate the procedure as the use of a guide and cannulated nail.

FIG 568 —The rod is strapped on to the normal thigh at the level of the femoral neck   A film is taken with the hip abducted and internally rotated   The length of the nail required is determined by measuring the shadow of the bone against the equally magnified shadow of the rod.

The Author's Operation.[12]—

Length of Nail.—The correct length of nail is determined with absolute accuracy before the operation is begun.   The surgeon must be sure that the nail is long enough to engage with the greatest possible depth of bone in the proximal

fragment. Equally he must be confident that the nail can be hammered home without penetrating the joint. If the head of the nail is not firmly punched into the cortex, the nail may slide out of the proximal fragment before the fracture is united (*see Figs.* 578, 579).

The X-ray shadow, being magnified, cannot be measured directly. Moreover, the degree of magnification depends on the distance of the tube from the limb, and standardized calculations are therefore fallacious. A measuring rod graduated with $\frac{1}{4}$-in. grooves has been made (*Fig.* 567). This is strapped on to the outer aspect of the thigh level with the neck of the femur on the uninjured side; the hip is fully abducted and internally rotated and a film is taken (*Fig.* 568). The true length of the bone may now be determined by measuring the shadow of the femoral neck against the equally magnified shadow of the grooved rod.

Operative Exposure.—Spinal anæsthesia is used except in cases of low blood-pressure. The neck of the femur is exposed in the interval between the gluteus medius and the tensor fasciæ femoris (*Figs.* 569, 570). To assist in retracting the gluteus medius sufficiently to see the side as well as the front of the neck, the anterior fibres of insertion are dissected off the trochanter. If a more free exposure is required an osteotome is driven into the front of the trochanter, which is levered out on its intact posterior margin (*Fig.* 571). Separation of the trochanter, however, involves a good deal of hæmorrhage, whereas if this is avoided the operative field is almost bloodless. The capsule is incised along the upper border of the neck, dissected away
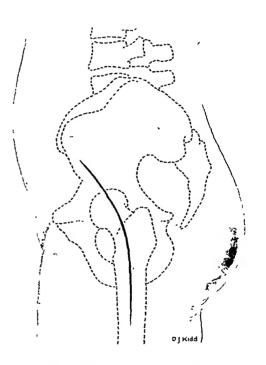
FI9. 569.—Lateral approach for open reduction.

from the intertrochanteric line, and turned forwards as a triangular flap. If the upper fibres of the vastus externus are now turned down subperiosteally, a wonderfully clear view of the whole line of the neck is secured.

Insertion of Guide and Reduction of Fracture.—The point of entrance of the guide is chosen exactly in the middle of the lateral surface of the femur $\frac{1}{2}$ to $\frac{3}{4}$ in. below the trochanter, and the cortex is perforated with a gouge to allow the guide to be driven in easily. The guide is bored in by means of a simple T-shaped handle (*Figs.* 572, 573) and is inserted and re-inserted as frequently as necessary until it is seen to emerge from the exact centre of the fractured surface. The fracture is now reduced accurately and the guide is driven into the proximal fragment. Since it is known that the guide lies in the middle of the distal fragment, it

is only necessary to secure perfect reduction of the fracture to be certain that the guide will enter the middle of the head.   Perfect reduction of the fracture is also of great importance because the final range of hip movement depends entirely on the accuracy of reduction.   If the fragments are too much impacted, the neck will be shortened and abduction movement limited.   If there is any rotational displacement, flexion movement will be limited exactly as it is in epiphysial coxa vara.   *Fig.* 574 illustrates the range of joint movement in a typical series of cases. Comparison of these photographs with the lateral radiographs shows that in every case
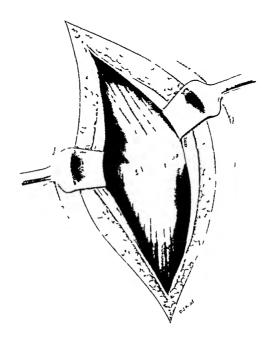
FIG 570 —The anterior border of the gluteus medius is defined and retracted outwards   The upper fibres of the vastus externus are turned down subperiosteally.

where hip flexion is limited there is some degree of rotational displacement, whereas in every case where hip movement is normal the fracture has been perfectly reduced.

The guide is of sufficiently heavy material to steady the fragments and to prevent re-displacement while the nail is being inserted.   The Smith-Petersen retractor, which is only insinuated with great difficulty between the articular surfaces of the joint, becomes unnecessary, and since it is an instrument which must aggravate the tendency to arthritis it should be discarded.

Insertion of Nail.—The nail is threaded over the guide and hammered in with a cannulated punch.   It is important to see that the guide engages accurately with the cannula of the punch and that it is not driven still further into the bone as the nail is hammered home (*see* p. 801).   If the fragments have separated slightly as the nail entered the proximal fragment, the gap is closed by the Smith-Petersen
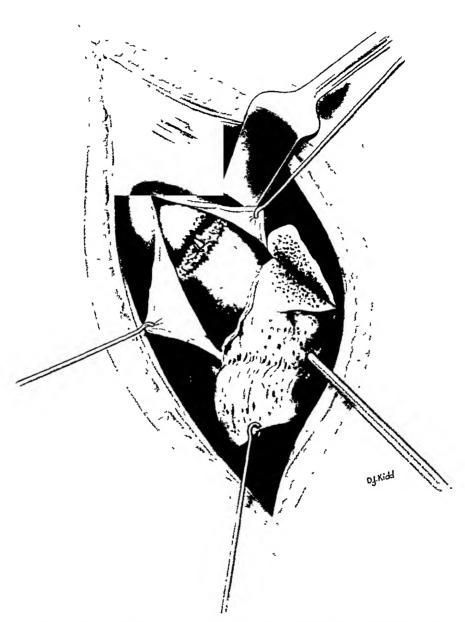
FIG 571.—For a more free exposure the front of the trochanter is levered out on its intact posterior margin   The capsule is turned down as a triangular flap to expose the whole length of the femoral neck   The point of the guide must be seen exactly in the middle of the fractured surface before the fracture is reduced.
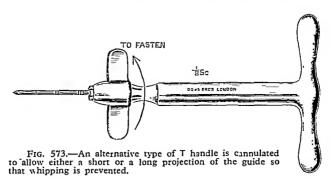
impaction punch.   This punch should be used very cautiously, and no more should be done than to close the gap.   Belief in the importance of impaction is a relic of the days when there was no other means of arresting rotational movement of the fragments.   Now that this movement is controlled by the three-flanged nail, these fractures unite just as certainly whether they are impacted or not. Blind and uncontrolled impaction is not only valueless, but it destroys the cancellous bone, shortens the femoral neck, and may increase the tendency to

FIG. 572.—The directing guide is held in a chuck which will fit either a T-shaped handle or a brace.   Direction can be more accurately controlled if the guide is bored in with the T handle; but if the bone is unduly hard, the guide is drilled in with a brace.

arthritis by bruising the articular surfaces.   Cautious use of the impaction punch is specially important if closed methods are used and the fracture is not visualized.

After-treatment.—No plaster spica or other external fixation is used.   A Thomas's splint is dangerous because it converts the limb into a long rigid lever which transmits every movement exactly to the level of fracture.   Moreover, knee movement must begin the day after operation.   Some simple measure should be used to prevent the limb from turning into the externally rotated position.   A shoe

FIG. 573.—An alternative type of T handle is cannulated to allow either a short or a long projection of the guide so that whipping is prevented.

or bedroom slipper with a 6-in. piece of wood nailed on to the heel and projecting outwards so that it lies flat on the bed is quite adequate.

In low transcervical fractures it is safe to begin weight-bearing in four to six weeks (*Fig. 575*).   In high subcapital fractures there should be no weight-bearing during the first three months nor until there is radiographic evidence that the fracture is uniting.   In most cases there is evidence of union in three or four months and of final consolidation in four to six months.   Even though weight-bearing is not allowed, the patient sits up and turns regularly in bed.   No more than this is necessary to avoid hypostatic congestion even in the oldest of patients, and early weight-bearing is not imperative.
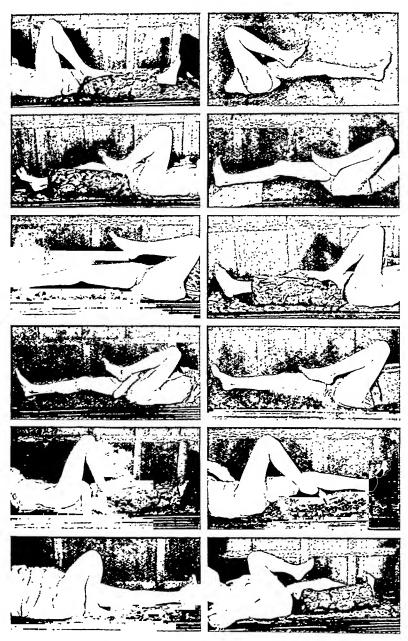
FIG. 574.—A typical series of end-results showing the best and the worst ranges of hip and knee movement. Limited hip flexion is always due to inaccurate reduction of the fracture (rotational displacement).

The Extra-articular Operation of Sven Johansson[6] and King.[11]—The fracture is first reduced on a traction table and the accuracy of reduction confirmed by antero-posterior and lateral radiographs. A 3- or 4-in. incision is used over the great trochanter and one or more Kirschner wires are drilled into the neck. Sven Johansson relies on mathematical calculations and an elaborate directing apparatus. King uses several wires, the first inserted behind the femoral neck under fluoroscopic control, and the others in the bone. Whatever devices are used to assist in directing the wires, antero-posterior and lateral radiographic control is essential and the nail is not introduced until one wire is seen to be in perfect position. Radiographs are again taken after the nail is inserted and the wire withdrawn.

Comparison of the Blind and the Open Operations.—Similar extra-articular methods have been used in a few patients who were thought to be too old
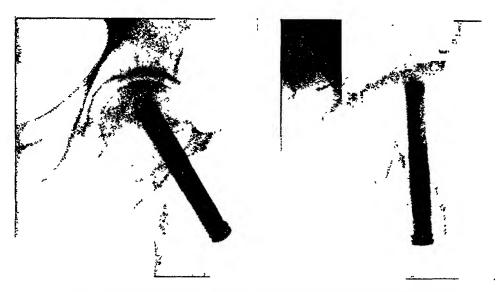
FIG. 575.—In transcervical fractures with an accurately placed nail weight-bearing may begin in four to six weeks. Early weight-bearing is not permitted in subcapital fractures.

and feeble for the open operation (one being an old woman of 91 whose fracture was successfully nailed). Local anæsthesia was used, with a very short incision just long enough to admit the nail and punch. No directing apparatus was employed but there was radiographic control throughout all stages. The procedure is a long and tedious one, the operative time varying from one to two and a half hours, whereas the open operation which has been described can be completed in thirty to forty minutes. The extra-articular method can only be carried out if a traction table, one or preferably two portable X-ray machines, and excellent team work and organization are available. It is by no means certain that this technique causes less shock than the open operation. With the 'open' procedure there is a 6-in. incision, rather more hæmorrhage, and a rapid operation; with the 'closed' technique a 2- to 4-in. incision, rather less hæmorrhage, and a prolonged operation. The one advantage of the blind method over the open one is the reduced risk of

sepsis, and King freely admits that this is the main reason for his advocacy of the extra-articular operation.

The position may therefore be summarized by saying on the one hand that no surgeon should attempt the extra-articular or blind operation unless he can command expert team work and radiographic control in the operating-theatre, and on the other hand, that no surgeon should attempt the open operation unless he can be quite confident of asepsis, and of a high standard of operative skill and judgement.

BASAL FRACTURES OF THE FEMORAL NECK

Since Whitman's work[13] was first published it has been possible to rely on good bony union of basal fractures of the neck of the femur treated in a plaster spica. For this reason the nailing operation has not been generally applied to fractures at this level. Nevertheless the plaster spica is associated with considerable difficulties and discomforts. Severe stiffness of the knee frequently develops, and unless the plaster is retained for four to six months coxa vara and shortening usually appear. Experience with high fractures has shown that the post-operative convalescence is so much more comfortable and so relatively free from complications, that during the last eighteen months we have been nailing basal as well as cervical fractures wherever possible.

Even greater difficulties may be experienced than in the nailing of high fractures. One of the first cases failed because the nail was inserted in the usual position $\frac{1}{2}$ in. below the lower margin of the great trochanter. At this level the bone of the distal fragment is usually too thin to secure a firm grip of the nail. Although the nail becomes firmly embedded in the proximal fragment it is still possible to move the distal fragment on the nail and the fracture is not completely immobilized. In later cases the nail has been driven in at a much lower level, usually $1\frac{1}{2}$ to $2\frac{1}{2}$ in. below the trochanter, so that it lies more obliquely and is buried in not less than 1 in. thickness of bone below the fracture (see Fig. 578). The shaft of the femur, however, is much more prone to splitting than the trochanter and neck, and the nail must be hammered in with great care. The tendency is to split upwards from the nail to the fracture, so that none of the three blades of the nail should point in this direction. Before the guide or nail is inserted a hole should be gouged out of the cortex only slightly less than the diameter of the nail. If a split does appear in the cortex its extension upwards must be prevented by making a small cross-cut with a fine osteotome or saw. Before embarking on the operative fixation of pertrochanteric and intertrochanteric fractures, lateral as well as antero-posterior radiographs must be carefully examined in order to be sure that the comminution of the upper femoral shaft will not prove an insuperable obstacle.

PATHOLOGICAL FRACTURES OF THE NECK OF THE FEMUR

An attempt was made in one case to nail a fracture of the neck of the femur in a case of osteitis deformans. In Paget's disease fractures of the femoral neck show the same interference with the blood-supply of the head, the same delay in union and tendency to non-union which is observed in uncomplicated cases. The

operation was undertaken with some reluctance, but since the bone had fractured and not bent, it was thought that the disease must have advanced beyond the stage of softening to the stage of recalcification. It seemed possible that a nail might succeed in immobilizing the fracture and overcoming the joint stiffness, which is particularly difficult in cases of Paget's disease immobilized in plaster. The operation was most difficult owing to the thickening and vascularity of the bone, and, moreover, with the last punch of the hammer the bone split down the whole length of the neck. The nail was withdrawn and a double plaster spica applied. The fracture did ultimately unite after six months of immobilization. Experience in this case discourages any further attempt to apply the nailing method to femoral neck fractures in Paget's disease.

In one other case there was a pathological condition of the bone which was not recognized before operation. The patient had previously sustained a fracture of the shaft of the humerus from a trivial injury, and the X-ray showed undue sclerosis of the neck of the femur but no evidence of a generalized skeletal disorder. When the fracture was exposed it was found quite impossible to drive the guide beyond the cancellous tissue of the trochanter into the neck, the bone of the neck being extraordinarily dense and hard. An attempt was made to drill the bone but this also failed. The nail was ultimately inserted with very great difficulty after a track had been cut with a narrow gouge.

FIG. 576.—Re-fracture three weeks after an apparently successful operation, with re-displacement and 'fore-shortening' of the neck due to external rotation. The nail though in good alignment lay marginally. A marginal fragment of bone has broken off the proximal fragment and lies above the point of the nail. The complication may now be avoided by the use of a guide and cannulated nail.

Twelve months later the lower half of the fracture is united, but there is decalcification and absorptive change in the upper half. It is proposed to remove the nail and apply a plaster spica for two to three months in the hope that consolidation will be completed. No evidence is yet available as to the underlying cause of the osteosclerosis.

COMPLICATIONS

Re-fracture due to Inaccurate Insertion of Nail.—This complication was only observed in the earlier cases of the series, but at that time it represented one of the great difficulties of the operation (*Fig.* 576). The use of a preliminary guide and the new exposure of the fracture has solved this problem. The introduction of Smith-Petersen nails without the use of a preliminary guide, and without either radiographic control or operative exposure of the fragments, should no longer be countenanced.

Wound Infection.—There was only one case in this series of 64 operations where there was any infection of the wound. The infection was of a low grade, but the formation of a sinus necessitated removal of the nail. The open operation should not be performed unless asepsis can be relied upon, and no-touch technique must be adopted exactly as in any other joint operation.

There was one other case, already referred to, of aseptic necrosis of the flap in a uræmic patient with auricular fibrillation. Since all of these patients are old and many have circulatory failure, flap incisions should be avoided.
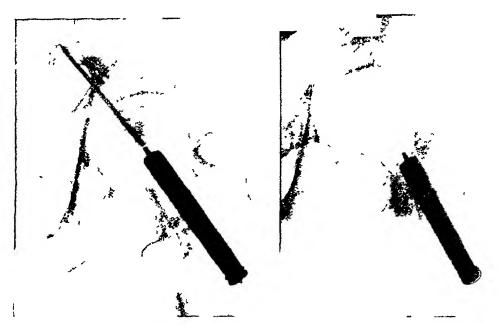
FIG 577.—Basal fracture after nailing The guide was inadvertently driven in with the nail Extraction of the guide was made still more difficult by its breaking in the middle of the femoral head just beyond the point of the nail

FIG 578 —Same case as Fig 577 after intra-abdominal extraperitoneal removal of the broken fragment of guide three weeks after first operation In basal fractures the nail is driven into the shaft at a lower level, in order to gain a firm grip of the distal fragment. The nail is beginning to slide out of the bone.

Penetration of Guide into Acetabulum and Pelvis.—In one case there was an unexpected complication which gave rise to serious difficulty. When the guide is in position in the femoral neck, the length of guide projecting beyond the bone may be less than the length of the nail, so that when the nail is threaded over it the guide is obscured. In this case the nail was punched home without first confirming the fact that the guide was threading satisfactorily through the cannula of the punch. Only when the nail was completely embedded was it discovered that the guide had gone right through the hip-joint and pelvis. It was impossible to extract it without extracting the nail. Radiographs showed that the situation was still more difficult, for the guide had fractured in the middle of femoral head just beyond the point of the nail (*Fig.* 577). The problem was to extract a 4-in. fragment of metal with one end in the middle of the femoral head and the other end in front of the sacro-iliac joint. It was successfully removed

three weeks later by an incision along the crest of the ilium and Poupart's ligament, stripping up the periosteum of the ilium, the iliacus and the peritoneum, localizing the guide in the true pelvis, cutting it in half, and extracting each half independently (*Fig.* 578). The patient recovered with no sign of damage to the hip-joint.

Now that this complication is recognized it is unlikely to recur. It is an easy matter when the nail is half embedded to be satisfied that the guide is passing smoothly through the cannula of the nail and punch.

Penetration of Nail into Hip-joint.—The use of too long a nail so that the point emerges through the articular surface of the femur was a constant fear in earlier cases. Several examples have been recorded. Now that the necessary length of the nail is calculated before operation, using the special graduated X-ray rod, and measuring the distance in the normal hip from a point $\frac{3}{4}$ in. below the lower margin of the great trochanter to a point $\frac{1}{4}$ to $\frac{1}{2}$ in. from the articular surface, this difficulty does not arise. In older cases where there has been absorption of the bone this measurement of the normal hip may be fallacious. In such a case the depth of the proximal fragment should be estimated before operation by the measuring rod, and the depth of the distal fragment measured during the operation. When the point of the guide has just appeared at the fractured surface the length of guide still projecting beyond the bone is measured and subtracted from the total length of the guide already known.
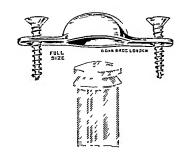
Loosening of Nail from Bone Absorption.—It might be thought probable that absorption of bone round the nail due to an irritative hyperæmic decalcification would account for frequent failure. Decalcification of such a degree as to endanger fixation of the fragments was only observed in the earliest cases when plated nails were used. With stainless steel nails there is very much less reaction. That there is some decalcification is undoubted,

FIG. 579.—Subcapital fracture three and a half months after nailing. Originally the nail was well embedded in the proximal fragment, but it has slid down its groove in the bone, leaving a small fragment of metal behind. Fortunately, the fracture had already united.

and the remarkable tightness of the nail when it is first driven in is not maintained for more than a few weeks.* After that time it is not difficult to slide

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* The fact that in post-mortem specimens the nail after the lapse of many months may still be so firmly gripped by the bone that it cannot be moved may prove misleading. The shrinkage of the adjacent bone as the post-mortem specimen dries is sufficient to grip the nail once more, and it does not follow that the nail was equally tight during the life of the patient.

the nail up and down its socket in the bone; but the genius of the invention lies in the fact that a three-flanged nail still lies in a three-grooved socket, so that rotational movement is still impossible and there is no interference with the consolidation of the fracture.

FIG 580.—Stainless steel domed cap which is screwed over the head of any nail which shows a tendency to slip out of the bone
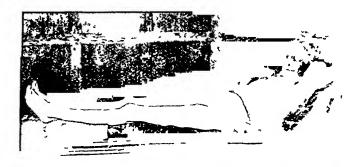
In many cases this longitudinal movement of the nail is of such a degree that the head of the nail becomes more and more prominent as it slides out of the bone, and tenderness over the nail head is one of the definite indications for removal

FIG. 581.—Cervical fracture showing the domed cap in position over a cannulated nail. The cap is not applied as a routine, but only after six or eight weeks if there is evidence of displacement of the nail

of the nail. This seldom occurs in less than six to twelve months, but in one case where the nail head had not been firmly punched into the cortex of the femur the nail slid down so rapidly that its point was disengaged from the proximal fragment as early as three months after operation (*Fig. 579*). Fortunately repair was rapid in this particular case and the fracture had already united. To meet this difficulty a stainless steel cap has been made (*Fig. 580*) which can be screwed over the head of the nail. It is not used as a routine, but is reserved for any case in which longitudinal displacement develops six or eight weeks after operation (*Fig. 581*).
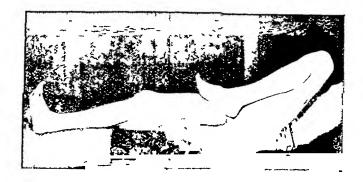
FIG 582 —An almost normal range of hip and knee movement may be anticipated if the fracture is perfectly reduced, and knee exercises are begun the day after operation

Joint Stiffness.—Most patients have no difficulty in retaining a full range of flexion of the knee provided that active movements are begun immediately after operation. No patient in this series had less than right-angled flexion, and most of them recovered full movement (*Fig.* 582).

The range of hip movement depends on the accuracy of reduction. In one case there was serious external rotation deformity and only 60° of hip flexion. The average range of hip flexion is from 90° to 160°, but it is always found, in cases free from arthritic change, that limitation of hip movement is due to inaccurate reduction. This provides one of the strongest arguments for the open operative method where the fragments are fully visualized, particularly in younger patients, and especially in working men.

Arthritis of the Hip-joint.—Not all of the cases in the series have been under observation for a sufficient number of years to know whether osteo-arthritis will develop or not. In one patient operated on within a few days of fracture there is severe arthritis with a painful stiff hip-joint three years after operation (*Fig.* 583). A second patient, operated on six months after fracture, has an equally severe arthritis. A third, operated on within three weeks, has slight arthritic change with some pain. In all of these cases the fracture was subcapital and there had been radiographic evidence of impairment of circulation of the proximal fragment. The complication is not entirely within the control of the surgeon, but its incidence may be minimized by operating early, by avoiding unnecessary hammering of the joint, by avoiding early weight-bearing, and by removing the nail after consolidation of the fracture.

FIG. 583.—Subcapital fracture of the neck of the femur three years after nailing, showing degenerative arthritis due to necrosis of the head following avascularity. The incidence of this complication may be minimized by operating early, by avoiding undue impaction, and by prohibiting early weight-bearing.

RESULTS OF TREATMENT

The 64 cases which have been operated on are considered in two series, the first from 1930 to 1933, when the Smith-Petersen technique was mainly used (29 cases), and the second from 1933 to 1935, when the author's technique was followed (35 cases) (*Tables I* and *II*). The first series suffered from the disadvantages of inexperience, and moreover it includes failures due to the use of plated nails. On the other hand, with extended experience an increasingly high proportion of cases have been operated on, and less and less promising material has been accepted as suitable. Whereas in the first series operation was performed in only half of the total fractures seen, in the second series 85 per cent of the fractures were treated

by operation.   These patients are not only old, the average age being 60, but they include many with serious constitutional disorders—chronic bronchitis, emphysema, circulatory impairment, auricular fibrillation, pernicious anæmia, enlargement of the prostate, and uræmia.   Even so, successful results were secured in 91 per cent of cases in the second series.

The operation mortality-rate of the whole group of 64 cases is 6 per cent, a mortality which compares very favourably with the general mortality of this fracture treated by all methods.   In 30 personal cases treated in earlier years before the introduction of the nailing operation there was a mortality of 14 per cent, and the combined figures of several voluntary and municipal hospitals in Liverpool and Manchester showed a mortality of 21 per cent in 61 cases.   There can be no doubt therefore that Smith-Petersen's discovery has not only revolutionized the prognosis of this injury from the point of view of union of the fracture, but it is also to be regarded as a life-saving measure.

Table I.—ANALYSIS OF RESULTS

Smith-Petersen Technique (1930–3).—

Total cases seen	..	59 (average age 57)
Cases operated on	..	29 (49 per cent)
Failed	..	4 (3 re-fractures, 2 plated nails)
Died ..	..	2
Bony union	..	23 (79 per cent)

Author's Technique (1933–5).—

Total cases seen	..	41 (average age 60)
Cases operated on	..	35 (85 per cent)
Excluding 3 atypical cases		
Failed	..	1 (sepsis)
Died ..	..	2
Bony union	..	29 (91 per cent)

Mortality of combined series—4 in 64 (6 per cent)

Table II.—DETAILED RESULTS IN BOTH SERIES OF OPERATIONS

PATIENT	AGE	SITE	RESULT	COMMENTS
Smith-Petersen Technique (1930–3).—				
E. E.	61	Cervical	Non-union	Plated nail. Absorption of bone
F. M.	21	Cervical	United	
A. S.	69	Cervical	Non-union	Plated nail. Absorption of bone
T. S.	34	Cervical	United	
P. K.	40	Cervical	United	Two nails used
F. R.	15	Cervical	United	
T. P.	40	Cervical	United	
E. S.	61	Cervical	United	
C. M.	60	Cervical	United	
de B.	70	Cervical	United	Re-fractured. Re-nailed (3rd week)
M. H.	78	Cervical	United	
M. M.	79	Basal	United	
J. S.	42	Cervical	United	
C. D.	56	Cervical	United	
E. W.	57	Cervical	Non-union	Re-fractured. Plaster spica (after few days)

Table II.—Detailed Results in Both Series of Operations, *continued*

Patient	Age	Site	Result	Comments
Smith-Petersen Technique (1930–3), *continued—*				
O. J.	49	Cervical	United	
C. S.	46	Cervical	United	
A. D.	57	Cervical	United	Head completely avascular. Slow union (12 months). Osteo-arthritis (*see Fig.* 582)
I. M.	65	Cervical	United	
M. W.	68	Cervical	United	
A. H.	70	Cervical	Died	Died 3½ weeks. Pneumonia
M. C.	78	Cervical	United	
F. M.	65	Cervical	United	
M. H.	67	Cervical	United	Re-fracture (5th week). Re-nailed (*see Fig.* 575).
E. F.	46	Cervical	United	
B. M.	64	Basal	Fibrous union	Nail too high in shaft
M. G.	55	Cervical	United	
B. J.	79	Cervical	United	
M. H.	65	Cervical	Died	Died 10th week. Flap sloughed. (Enlarged prostate, uræmia, auricular fibrillation)
Author's Technique (1933–5).—				
S. M.	52	Cervical	United	
M. B.	75	Cervical	United	
C. C.	75	Cervical	Died	Died 3rd day. Very feeble constitution
M. A.	72	Cervical	United	Pernicious anæmia. Recently cured tuberculosis of lumbar spine (*see Fig.* 578)
E. W.	57	Cervical	Non-union	Sepsis. Low-grade infection—sinus. Nail removed. Plaster spica
F. M.	20	Cervical	United	
W. H.	44	Cervical	United	
E. G.	47	Cervical	United	
J. P.	73	Basal	United	Guide broke off in pelvis. Extracted 3 weeks later, abdominal route (*see Figs.* 576, 577)
E. McC.	57	Cervical	United	
W. G.	60	Cervical	United	
E. R.	58	Cervical	United	
S. W.	45	Cervical	United	
P. B.	91	Basal	United	Local anæsthetic. Subcutaneous insertion with X-ray control
A. D.	59	Cervical	United	
M. A.	74	Cervical	United	
E. P.	58	Cervical	Died	Died 1st day. Shock
P. L.	33	Cervical	United	
L. H.	60	Cervical	United	
C. N.	45	Cervical	United	
A. L.	65	Cervical	United	
M. D.	65	Basal	United	
A. S.	75	Basal	United	Shaft comminuted. Plaster spica after 10 days
M. O.	70	Cervical	United	Epileptic. Very frail. Local anæsthetic and subcutaneous insertion with X-ray control
G. T.	72	Cervical	United	
?	60	Cervical	United	Pernicious anæmia. Blood transfusion before operation
J. K.	78	Cervical	United	
S. A.	65	Cervical	United	
W. G.	60	Cervical	United	Severe poliomyelitis same limb
E. A.	72	Basal	United	
J. P.	46	Cervical	United	

Table II.—DETAILED RESULTS IN BOTH SERIES OF OPERATIONS, *continued.*

PATIENT	AGE	SITE	RESULT	COMMENTS
Atypical Cases.—				
E. T.	48	Cervical	Uniting	? Osteosclerosis. Previous spontaneous fracture humerus. Neck of femur extraordinarily dense. Still under treatment (partly united despite absorption upper half of fracture). (*See* p. 800)
S. C.	60	Cervical	United	Paget's disease. Neck of femur split. Nail removed. Plaster spica 6 months. United. (*See* p. 799)
M. C.	61	Cervical	United	7 months old. Aseptic necrosis of head. Nail gradually displaced. United after 18 months. Severe osteo-arthritis. Stiff painful hip. (*See* p. 789)

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TWO CASES OF CYSTADENOMA OF THE PANCREAS

By ROBERT M. JANES

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF TORONTO, AND THE TORONTO GENERAL HOSPITAL

CYSTADENOMAS of the pancreas are sufficiently rare to justify the placing on record of individual cases. According to Miller (quoted by Huefer) only twenty-four cases were reported up to 1926, and there would appear to have been few additions to the literature since that time. The two cases that form the basis of this report came under the care of the writer within a comparatively short period and are the only ones that occur in the records of the Toronto General Hospital.

Case I (No. 081890).—Miss L. R., aged 70.

HISTORY.—Admitted on Oct. 15, 1933. Five years previously while massaging her abdomen to relieve constipation she noticed what seemed to be a small lump in the epigastrium. For three years the lump had remained barely palpable; it had enlarged slowly from that time. For the past two to three years she had been troubled with belching of gas and flatus, but during the past few months these symptoms had increased and had been accompanied by epigastric discomfort and water-brash. For one month she had had attacks of sharp pain that encircled the body at about the level of the umbilicus. An habitual constipation had increased recently. Two to three weeks previously her stools had been almost white for a few days. The appetite was poor, and eating was followed by discomfort and occasionally by vomiting. In the first eighteen months of the past two years there had been a loss in weight of about 6 lb., and in the past six months a loss of 40 lb.

ON EXAMINATION.—Although not in apparent distress, the patient was pale, very thin, and looked ill. A firm somewhat irregular mass filled the whole epigastrium. It was only slightly tender, moved with respiration, and did not seem to be attached to the liver, the lower edge of which was palpable 1 in. below the costal margin. Barium series and barium enema showed no intrinsic lesion of the stomach or colon. The pyloric end of the stomach and the duodenum were pushed downward and to the left, the displacement produced being such as would result from a retroperitoneal mass in the region of the head of the pancreas. The iodekon test showed a malfunctioning gall-bladder, and the leucocyte count was 10,000 per c.mm.

It was felt that the diagnosis lay between a cyst of the pancreas, a cyst of the liver, a carcinoma of the pancreas, and a mass of retroperitoneal glands, and that a laparotomy was necessary.

FIRST OPERATION (Oct. 19, 1933).—Spinal anæsthesia supplemented by gas and oxygen. Right paramedian incision. The mass was found to be a multi-loculated cyst of the pancreas about the size of a large orange. It projected forward above the pylorus and first part of the duodenum and displaced the common

bile-duct to the right and the portal vein to the left (*Fig.* 584). The hepatic artery passed above and the pancreatico-duodenal artery round the right side of the tumour. The liver and gall-bladder appeared to be normal and the common bile-duct was not dilated. Removal of the cyst, although obviously difficult, seemed possible, and because the symptoms were increasing it was decided to attempt it.

The gastro-hepatic omentum was divided. The adjacent structures were separated slowly from the mass. The portal and superior mesenteric veins were especially difficult to free because they were bound to the cyst by innumerable bands of fibrous tissue which lay between the surface loculi and carried great numbers of small blood-vessels. A pedicle about 2 in. by ½ in. was finally obtained,
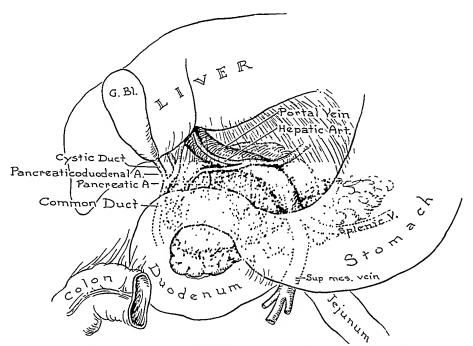
FIG. 584.—*Case* 1. Showing approximately the position of the tumour and its relation to surrounding structures.

but beyond this point the growth seemed to shade imperceptibly into pancreatic tissue. It was feared that further dissection might result in damage to the main duct of the pancreas. The pedicle was clamped, cut across, and oversewn with plain catgut. The abdomen was closed about a rubber drain containing plain gauze carried down to the bare area of the pancreas. Despite the fact that the operation had lasted for three hours the patient's condition was fairly satisfactory. A transfusion of 400 c.c. of blood was given.

There was remarkably little post-operative reaction, the maximum temperature being 101·5° and the pulse 100. The drain was removed on the fifth day. Considerable clear mucoid discharge containing pancreatic enzymes continued to come from the opening until Nov. 12, twenty-three days following operation. She was discharged on Nov. 20 free of symptoms but with a firm lump the size of a lemon in the region of the original mass.

RE-ADMISSION (Feb. 12, 1934).—The patient had remained free from symptoms until three weeks previously, when she had had an attack of generalized crampy abdominal pain. She was again well until three days before admission, when a similar attack of pain occurred, this time accompanied by vomiting. The temperature was 100°, pulse 100, and leucocyte count 23,000. The abdomen was slightly distended and in the upper right quadrant there was rigidity and tenderness. A tender mass could be felt in the right loin, but because of the rigidity and

FIG 585.—*Case 1.* Adenocystoma of pancreas. Photograph of gross specimen.

tenderness it could not be definitely outlined. A diagnosis of recurrent pancreatic cyst was made.

SECOND OPERATION (Feb. 15, 1934).—Gas and oxygen anæsthesia. A 2½-in. incision was made directly over the swelling. A pear-shaped mass, 3 × 3 × 5 in. was exposed, the base presenting. Opalescent fluid was obtained from it with a needle. The cyst was found to be unilocular and to have a wall about 3 mm. in thickness. It was marsupialized.

SUBSEQUENT PROGRESS.—Recovery was rapid and uneventful. The fluid discharged from the sinus was at first brownish in colour, but soon became clear

and watery in character; it contained pancreatic enzymes in small quantities. On March 11 the sinus was injected with lipiodol; no communication with the pancreatic ducts could be demonstrated. The patient was discharged on March 12 with a small drainage tube *in situ.*

Normal weight was regained rapidly. The escaping fluid gradually lessened in amount and became more mucoid in character. Temporary cessation of the discharge was on several occasions accompanied by pain. The opening finally closed about Jan. 15, 1935. There has been no further pain, no mass can be palpated, and the general health remains excellent.

PATHOLOGICAL REPORT.—This material consisted of a multiloculated cystic mass of tissue measuring overall 6 × 6·5 × 7 cm. to which was attached a small piece of normal pancreatic tissue (*Fig.* 585). The cysts were all thin-walled and varied from 1 to 3 cm. in diameter. They were filled for the most part with a clear watery fluid, but in some the fluid was slightly blood-stained. On cross-section the cut surface of the attached pancreatic tissue was reddish grey in colour and there were dense bands of pearly white fibrous tissue traversing it.

Microscopic sections (*Figs.* 586, 587) of the wall of one of the smaller cysts showed that it was made up of a rather loose areolar type of connective tissue lined on its inner surface by a very thin layer of cuboidal epithelial cells.

Case 2 (No. 090502).—Mrs. M. D., aged 29 years.

HISTORY.—Admitted on June 13, 1934. During the past three years the patient had suffered about once a month from an attack of severe colicky pain in the right upper quadrant of the abdomen. The pain radiated to the back and both shoulders and was accompanied by nausea and vomiting. She thought she had been slightly jaundiced following each attack. During the last attack, three weeks previously, there had been chills and sweating. The pain bore no relation to any particular type of food and there was little food intolerance. She suffered from a bitter taste in her mouth, belched considerable gas, and said she felt as though food " stuck in her mouth ". She had recently lost 9 lb. in weight.

ON EXAMINATION.—The patient was thin and pale. The hæmoglobin was 72 per cent and leucocyte count 7200. The abdomen was scaphoid. A mass which appeared to be rounded and about 1 in. in diameter could be seen to descend with each inspiration along the upper part of the lateral margin of the right rectus. It was not readily palpable and was slightly tender. A diagnosis of chronic cholecystitis and cholelithiasis was made.

OPERATION (June 16, 1934).—Spinal anæsthesia. The abdomen was opened through a right paramedian incision. A mass the size of a large walnut presented within the curve of the duodenum. It was dark green in colour, firm but resilient as though cystic in character. It was found to originate from and to have largely replaced the head of the pancreas. A very thin layer of overlying pancreatic tissue was incised and the cyst easily enucleated with but slight bleeding. The pancreatic ducts were not encountered. The dead space was obliterated, the opening in the pancreas closed, and the peritoneum sutured over this with fine plain catgut. The gall-bladder was slightly thickened and there were a few pericholecystic adhesions, but no calculi. The ducts were normal. The liver showed moderate cirrhosis. The gall-bladder was removed and the abdomen closed without drainage.

Convalescence was uneventful and she was discharged on July 3, 1934.

FIG. 586.—*Case* 1. Microscopic section of tumour. (× 40.)

FIG. 587.—*Case* 1. Microscopic section of tumour. (× 80)

FIG. 588.—*Case 2.* Microscopic section of tumour. (× 40.)

FIG. 589.—*Case 2.* Microscopic section of tumour. (× 80.)

PATHOLOGICAL REPORT.—The gross specimen consisted of a multiloculated cystic mass, roughly spherical in shape, measuring 2·5 cm. in diameter and weighing 6·8 grm. It was filled with a clear watery fluid.

Microscopically (*Figs.* 588, 589) the cyst wall itself was quite thin, being made up of dense fibrous tissue lined on its inner surface by a single layer of somewhat flattened epithelial cells. A portion of adjacent pancreatic tissue included in the section showed no pathological change.

For the pathological descriptions and the photomicrographs I am indebted to the Department of Pathology of the University of Toronto.

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PROSTATECTOMY WITH CLOSURE:
ADDENDA AND SOME OBSERVATIONS

By S. HARRY HARRIS

HONORARY UROLOGIST, LEWISHAM HOSPITAL, SYDNEY

Two years ago the writer[1] described in this JOURNAL his operation of "Prostatectomy with Closure". Certain modifications have been introduced since that time as set forth below.

Gauze swabbing in order to obtain adequate visualization of the prostatic environs after prostatectomy has always appeared to me to be somewhat of an anomaly. Recently I have succeeded, with the assistance of the Genito-Urinary Manufacturing Company of London, and of Leiter of Vienna, in providing suction through the posterior blade of my electrically-lighted self-retaining retractor. In its latest form (*Fig.* 590, *a, b*) this instrument is of simple construction and only slightly heavier in weight than its plain-blade predecessor. It effects immediate evacuation of any overflow of blood from the prostatic loge.

In order to complete the visualization, a separate and most efficient metal tube-sucker has been constructed for me (*Fig.* 591). It is multi-curved in such a way that it may be insinuated by the assistant from any position into the prostatic loge with a minimum of inconvenience to the operator, so that, with the instruments I employ, vision at practically all times remains unobstructed. The necessity for gauze-swabbing has thus been eliminated and the operation time considerably curtailed.

The curved-tube sucker may be used with advantage even without the sucker-blade, but the combination of the two lends a nicety of technique not otherwise obtainable.

This dual suction at operation was first successfully employed by me at Glasgow and Edinburgh in October and in Vienna in November, 1935. Earlier in the year opportunities had been afforded me, in various London hospitals, of demonstrating my method of prostatectomy with immediate closure. Throughout my entire tour it was my experience that the majority of surgeons were content to submit patients to prostatectomy in whom the bladder had not been cleaned up to the extent to which we have been accustomed in the Urological Department of the Lewisham Hospital, Sydney, and which is readily attainable by the methods we have for several years practised and previously described in detail, both in this JOURNAL and elsewhere. Particular reference may, perhaps, be made here to our simple permanganate-of-potash–nitrate-of-silver method of bladder preparation, with the retained catheter connected by rubber tubing to a partially filled bottle at the bedside instead of into a urinal between the patient's thighs. It was possible on several occasions to demonstrate the efficiency of this treatment on patients who had had already a long period of preparation. The rapid conversion of a turbid urine into one with a crystalline appearance was very striking, enabling, as it did, the safe undertaking both of the plastic procedure on the bladder base and of the primary closure.
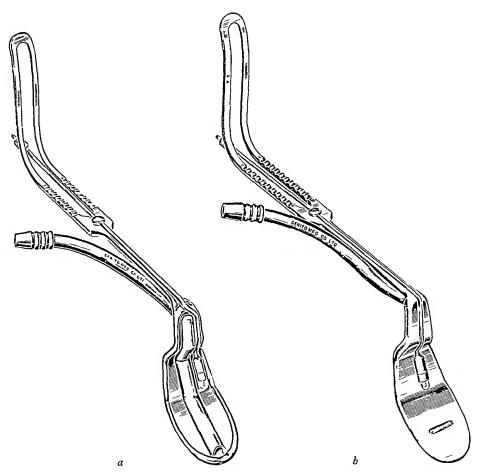
FIG 590 —Posterior sucker-retractors to fit author's self-retaining frame, made (a) by Leiter, Vienna, (b) by the Genito-Urinary Manufacturing Company, London Either may be employed with satisfaction (*Reduced about ¼ and drawn obliquely*)
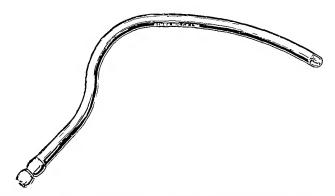
FIG. 591 —Individual sucker-tube made for the author by Leiter, Vienna.
(*Reduced by more than ¼*)

So far as the *retrigonization* was concerned, this would appear to have been carried out by many surgeons in accordance with my original description. The simplified technique, however, described by me in the opening address on 'Prostatectomy' before the Royal Australasian College of Surgeons in Adelaide, in January, 1934, was, not unnaturally, unknown. With this technique it is *not* necessary to pick up with forceps the floor of the prostatic capsule before passing the boomerang needle in order to ensure a satisfactory retrigonization. The needle is now entered
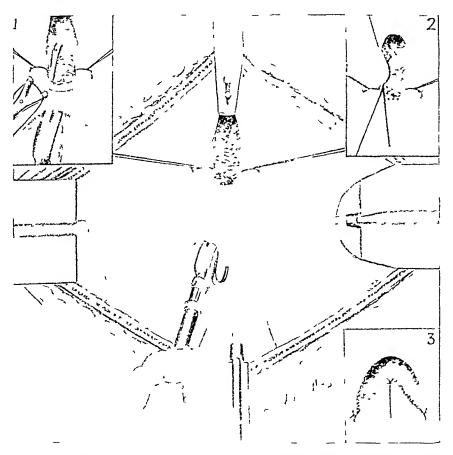
FIG 592 —Illustrating the retrigonization of the prostatic urethra   The main figure shows the point of entry of the needle in the bladder base well down behind the inter-ureteric bar   Insert 1 shows the point of emergence of the needle well forward in the prostatic cavity and the suture carrier approaching the needle   Insert 2 shows the retrigonization suture being tied, with the forefinger of the left hand pressing the loop well down into the prostatic cavity   Insert 3 shows the retrigonization suture tied, sewing the trigone well down into the prostatic cavity, both obliterating the ledge in this situation and re-forming, at least in part, the new prostatic urethra   Two haemostatic sutures only are illustrated in all figures for the sake of simplicity

in the mid-line at the deepest part of the ' bas fond ' (*Figs* 592, 593). It is, of course, necessary to visualize the ureteral orifices at this stage. No fear need then be entertained of compressing them when the suture is tied. The point of emergence of the needle is well down through the floor of the prostatic cavity (*Figs.* 592, 593). A wide and deep extent of tissue is, with ease and certainty, included in the bite of the needle. No attempt is, or ever has been, made by me to pick up in this bite the torn end of the prostatic urethra.

With regard to the *anterior transverse sutures*, there was a considerable degree of misconception. I consider the method and the site of insertion of these sutures as I have described them are vital features of the operation. With this technique there is no tendency to strangulation of the inverted prostatic rim with later sloughing and secondary hæmorrhage. The points of entry and of exit of these sutures are from 1 to 1½ in. from the free edge of the prostatic rim, the variation depending on the size of the prostatic cavity. The first, or more anterior suture, crosses the bladder base and the bottom of the prostatic cavity transversely and in a plane tangential to the anterior segment of the prostatic rim. This suture is immediately
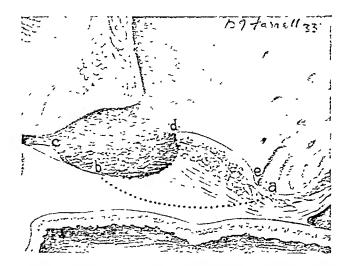
FIG. 593.—Illustrating the needle track, *a–b*, for the retrigonization suture. A sectional view of the prostatic environs after prostatectomy. *a*, Point of entry of the needle; *b*, Point of exit; *c*, Verumontanum; *d*, Torn apex of trigone; *e*. Base of trigone.

tied and converts the prostatic rim into a narrow oval. The second suture bisects this oval.

The catheter should on no account be passed before insertion of these sutures, as the catheter in the urethra presents an effective bar to the deep passage of the boomerang needle essential to secure for these sutures the necessary extent of bite. The tying of these sutures automatically brings about a broad, deep and smooth inversion of the prostatic rim and adjoining bladder base, while at the same time raising its level, thus securing: (1) Efficient obliteration of the prostatic cavity and venous oozing therefrom; (2) The re-formation in large degree of the side walls of the newly-formed urethra; and (3) A position for the new vesical outlet well below the level of the rest of the bladder base. The importance of the last-named both for the immediate catheter drainage and later for natural micturition cannot be over-estimated.

REFERENCE

[1] HARRIS, S. H., "Prostatectomy with Closure", *Brit. Jour. Surg.*, 1934, Jan., 434.

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EXPERIMENTAL SURGERY

INTESTINAL   STRANGULATION*

By G. C. KNIGHT and DAVID SLOME

LEVERHULME RESEARCH SCHOLARS, RESEARCH DEPARTMENT, ROYAL COLLEGE OF SURGEONS OF ENGLAND

THE problem of 'acute intestinal obstruction' has for many years stimulated clinical and experimental investigation, yet it is a depressing fact that the mortality-rate still fails to show any great decrease commensurate with the effort which has been expended on this problem. The series of 1000 cases collected from the literature over the ten-year period 1888–98 by Charles L. Gibson[1] showed an average mortality of 43·2 per cent. Recently Christopher and Jennings[2] have published a composite series of 2345 cases, including the above, with an average mortality of 46·5 per cent. Recent series which exclude paralytic ileus and mesenteric thrombosis show a mortality in the region of 31 per cent—such as the series of Souttar[3], 3064 cases, mortality 32 per cent; McIver,[4] 335 cases, mortality 31 per cent. One great lesson may be learned from a study of the statistical tables —the extreme urgency of the earliest possible diagnosis and treatment in reducing the mortality. For the rest they provide a great stimulus to investigation. It cannot be too strongly insisted that the term 'acute intestinal obstruction' is only a general one, covering a variety of pathological conditions, in some of which at least, *the obstruction per se is the least important factor*. Insistence must be laid on the correlation of clinical, experimental, and statistical findings with a definite type of pathological lesion, and the application of the results obtained in the investigation of one group to that group only, and not to the subject as a whole.

It has long been recognized clinically that a difference exists between intestinal obstruction and acute intestinal strangulation. They differ in their pathology, symptomatology, and mortality-rates. In both conditions the gut is usually obstructed, but in the former group—intestinal obstruction (due to causes such as neoplasms, gall-stones, foreign bodies, enteroliths, kinks, and band compression) —obstruction occurs without circulatory involvement. Such cases, excluding neoplasms, represent about 20 per cent of the total (Hausler and Foster[5]). McIver[1] reports 37 per cent in a series of 395 cases. Patients with such a condition *after a period of days* may exhibit an almost normal temperature, pulse-rate, and blood-pressure. Their general condition is good, and, despite pain and distension, their ultimate collapse is delayed for a period which varies with the position of the obstruction, only occurring early if this is high in the region of jejunum or duodenum, and delayed possibly for weeks if it is in the large intestine.

In the second group—acute intestinal strangulation (due to such causes as

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volvulus, internal strangulation, hernia, intussusception, band strangulation, etc.)—the essential pathological feature is venous strangulation of the intestine. Such cases represent 80 per cent of the total in Hausler and Foster's series and 63 per cent in McIver's[4] series. Sir David Wilkie[6] has said: "We are all familiar with the striking picture of shock and collapse which follows hard on the onset of strangulation of the intestine." In a period of hours the blood-pressure and body temperature fall profoundly, the pulse is rapid, the skin cold and clammy, and, if left untreated, such a patient may well be dead in a period at which a patient with simple obstruction at the same level would still be in good condition. McIver[4] regards this factor of strangulation as being of greater importance than the position of the obstruction. "It is generally recognized that obstructions of the colon are less fulminating than those of the small intestine. Of course, however, if interference with the mesenteric circulation be present, death will occur as quickly in one situation as the other."

As regards the mortality-rate, McIver, in a series of 156 cases, gives the percentage of mortality as 53 where there is interference with the mesenteric circulation, and 37 in simple obstruction. Over a thirty-year series of 395 cases, the figures are 62 and 38 per cent respectively. One set of figures will be cited out of many which illustrate the urgency of early diagnosis—those of Christopher and Jennings[2] (Table I).

Table I

DURATION OF SYMPTOMS BEFORE OPERATION	MORTALITY	
	Volvulus	Adhesions
	Per cent	Per cent
Less than 24 hours ..	0	0
24–48 hours	33·3	30
Over 48 hours	80	36
Not stated	100	14·4

From these facts it might be suggested that the greatest mortality arises where the gut is not only obstructed but also strangulated, and the process has been present for some length of time. Yet in the past by far the greatest volume of experimental effort has been directed to the investigation of intestinal obstruction without strangulation by such procedures as simple ligature of the intestine in continuity, double ligature at two points, division and re-suture without restoration of continuity, and formation of an isolated closed loop with restoration of continuity. In particular, attention has been focused on simple high obstruction of the small gut, the great infrequency of which may be judged from the fact that McIver could find only 3 examples without any vascular involvement in a series of 335 cases. It is therefore felt that any further investigation should be directed specifically to the problem of the circulatory collapse of intestinal strangulation, as opposed to simple obstruction. It is not intended to present a complete review of the exhaustive literature on simple intestinal obstruction, numerous résumés having appeared from time to time.[7, 8] Since in all our experiments the strangulation is associated with obstruction, it is important to realize what effects the obstruction alone might produce.

A few of the predominant points must therefore be summarized. Three theories have been advanced to account for the ultimate collapse of simple obstruction: (1) Reflex nervous action from the obstructed gut; (2) Bacterial invasion of the body from the same source; (3) A toxæmia.

Little real evidence has been advanced in support of the first theory, and it has been shown repeatedly that death may occur in the absence of any bacterial invasion of the peritoneum. In such cases cultures from the blood and viscera are sterile.[9, 10] The consensus of opinion is in favour of the third theory, but the origin and nature of the poisonous substance are by no means agreed upon. Clairmont and Ranzi[11] first showed that the content of an obstructed segment was toxic, but produced no evidence of its absorption. Cannon and Dragstedt[12] also hold that the toxin is elaborated from the content and is absorbed. Stone[7] holds a similar view. Whipple and his co-workers,[13] however, believe that the toxin results from an altered secretion of the intestinal mucosa, being partly secreted from it into the lumen, and in part absorbed into the blood-stream. As regards the nature of the toxin, there are also differences of opinion. Yet of the substances named, all might result from degradation of protein or similar large molecular substances. Sweet, Peet, and Hendrix[14] point out that such a process would result in the production of toxic proteoses and amines, while fat-splitting enzymes would produce from lecithin toxic cholines and neurines. We find that Whipple claims that the intoxication is due to a proteose.[15] Nesbitt[16] believes that neurines and cholines are significant, and Gerard[17] states that the substance is histamine (which Abel and Kubota[18] believe to be normally present in the digestive tract). Stone is of the opinion that a whole series of such split products are present in obstructed bowel, and possibly active in producing the lethal result. How such substances appear in the content, whether from bacterial activity[17, 19] or digestive action, is uncertain. Whipple[13] believes that neither bacterial nor pancreatic activity is significant, but that a proteose is secreted from the mucosa. Eisberg and numerous other workers, however, have demonstrated a greater toxicity of the loop content in the presence of digestive enzymes, and increase in the survival time if pancreatic secretions are excluded. Can this be of significance in relation to the greater toxicity of simple obstruction at the higher levels of the intestine? That such a difference in toxicity exists is shown by the survival times. Whipple, Stone, and Bernheim,[13] using washed and closed duodenal loops with restoration of continuity, gave an average survival time of forty-eight hours. Von Baracz[21] showed that closed loops of ileum and colon were very slightly toxic, dogs living for weeks or even months.

Of great importance is the time of appearance of the toxin. In all cases of experimental intestinal obstruction without strangulation, a definite interval elapses before much fluid collects in the loop and a still longer period before toxicity can be demonstrated in the gut content—Stone[22] gives these periods as 20 and 36 hours respectively. A summary of the available figures is given in *Table II*.

The presence of a toxin within the gut lumen has no significance whatever, if there is not positive evidence of its absorption. Although the toxicity of the loop content on intravenous injection has been amply demonstrated, Whipple[13] has shown that the injection of a double toxic dose of loop content into the lumen of a second obstructed loop does not accelerate the fatal outcome, and goes so far as to state that nothing produced inside the lumen of the intestine can be concerned

in the intoxication of intestinal obstruction, as such substances cannot be absorbed through intact mucosa. Cannon and Dragstedt[12] agree with this selective protective action, but believe that with *distension* and its resulting circulatory disturbance and tissue necrosis, absorption does take place. Brooks, Schumacher, and Wattenberg[27] also regard distension and necrosis as important factors in absorption, though not necessary for the actual production of toxin which is formed within the lumen. If distension is such an important factor, we have an alternative basis of explanation of the difference between high and low obstruction, for Murphy and Brooks[33] have demonstrated the more rapid secretion, and therefore more rapid distension, of high loops as compared with those that are prepared lower down in the intestine.

Table II

REFERENCE	TIME OF APPEAR-ANCE OF TOXIN	SITE	LEVEL OF OBSTRUCTION
Whipple[13] ..	24 hours	Mucosa	High closed loop
Stone[22]	36 hours	Lumen	High closed loop
Braye[23]	36 hours	Lumen	High closed loop
Dragstedt[25] ..	48 hours	Lumen	High obstruction
Van Beuren[21] ..	48 hours	Lumen	Simple jejunal ligature
Von Albeck[43] ..	24–48 hours	Lumen	Level not specified
Clairmont and Ranzi[11]	5 days	Lumen	Level not specified
Kukula[12]	3–10 days	Lumen	Level not specified

Saito[44] gives the period as 43 hours to 5 days according to the level, the toxin appearing earlier in the higher obstructions.

That a toxin does in fact appear in the blood, whatever its source, has been demonstrated. In 1909 Sauerbruch and Heyde[28] by a cross-circulation experiment were able to produce toxic symptoms in a normal animal as the result of intestinal obstruction in another. Sugito[29] has shown that the blood from the mesenteric veins draining the closed loop of intestine in a dog, if taken at the point of death, contains a toxic substance. This substance, *which is of the nature of a proteose,* is toxic on intravenous or intraperitoneal injection, in contrast to control injections of normal blood, and may be recovered from the spinal medulla, suggesting that it possesses a special affinity for nerve-cells. Scholefield[30] has confirmed the presence of this substance—again only in the terminal stages of closed-loop obstruction. It will be noted that in both these cases the experiments were conducted on closed loops, which are especially favourable to the occurrence of distension and its associated circulatory disturbances and necrosis. In Scholefield's post-mortem records such changes are specifically mentioned in 3 out of 4 cases. Although South and Hardt[31] believe that distension is not essential in the production of toxæmia, the recent work of Taylor, Wild, and Harrison[32] demands great attention. Introducing a rubber tube surrounded by a balloon into the intestinal lumen, they were able to produce distension of the gut without obstruction. X-rays demonstrated the passage of barium meal through the tube, but on distension of the balloon to a pressure of 100 mm. Hg, the animals succumbed in twenty-four hours with all the symptoms of experimental obstruction. These observers believe the distension produces this result through a nervous mechanism. A pressure of

100 mm. Hg, however, must necessarily cause venous occlusion, circulatory disturbances, anoxemia, and resulting changes in the tissues. In fact, it may produce certain of the characteristics of strangulation, which, as we shall show later, results in the rapid production of toxic substances and their appearance in the blood. It is, therefore, possible that the toxin which is found in the blood in the later stages of closed-loop obstruction may have had its origin in one of two sources : (1) Autolytic changes in the tissues of the gut wall itself—possibly resulting from anoxæmia, secondary to distension; or (2) The absorption of substances formed in the intestinal lumen.

Certain biochemical changes also support the presence of a toxin in the blood. Cooke, Rodenbaugh, and Whipple[34] have demonstrated a rise in the non-coagulable nitrogen of the blood in the presence of experimental intestinal obstruction, reaching three to ten times the normal figure at the height of the intoxication. A similar rise was produced by injection of toxic proteose, which Whipple[13] believed was secreted by the intestinal mucosa. They also demonstrated a rise in blood-urea and blood-creatinin, which they considered was due to protein or tissue destruction rather than impaired elimination.

The occurrence of dehydration and dechlorination is well known. Hartwell and Hoguet[10] noted the marked dehydration which occurred in obstructed animals after seven days' survival, and which they attributed to the associated vomiting. The dechlorination has been variously ascribed to loss by vomiting,[35] or, as suggested by Herrin and Meek,[36] to increased secretion, the result of distension, with chloride loss into the bowel lumen. Haden and Orr[37] suggested that the chloride is in part used up in the neutralization of toxic substances in the blood. Much has been written of the importance of dechlorination and dehydration in determining the fatal outcome, but experiments in which a fatal result has been directly produced by artificial dechlorination and dehydration are hard to find. Taylor and his co-workers produced this dechlorination by means of apomorphine vomiting, and conclude that their experiments in which " the blood chlorides were maintained at low levels for many days without serious effects resulting, must throw great doubt upon the primary importance of chloride loss as the cause of death in obstruction."

From these results it will be seen that the main evidence is in favour of death from simple obstruction being due to a toxæmia, the result of protein degradation occurring either in the bowel lumen or in the wall of the obstructed segment. A close corollary exists between the experimental and clinical picture in regard to the latent period before the onset of the toxæmia, forty-eight hours to five days, and to some extent in the greater severity of the high obstructions of the small intestine, although, as McIver has demonstrated, this latter point is less striking in the human than in the experimental animal.

It is in relation to this latent period that a difference exists between simple obstruction and acute intestinal strangulation. Murphy and Vincent[38] first demonstrated this point. Working with cats they prepared 12- to 15-cm. intestinal loops, from which the venous return was obstructed either by individual ligature of the veins or compression of the mesentery by a rubber ligature. They were able to demonstrate by blood-pressure records that the height of the toxæmia was reached in a period of four to six hours, at which time animals with simple obstruction (i.e., without venous obstruction) were quite unaffected. If, however, the

arteries were occluded as well as the veins, producing total anæmia, there was no such rapid intoxication. These results were confirmed by survival experiments. The results are shown in *Table III*.

Table III

LESION	POSITION	SURVIVAL TIME
Simple obstruction ..	High	4 days
	Low	7 days—killed
Total anæmia ..	High	3 days
	Low	2 days
Strangulation ..	High—5 cases	23–26 hours
	Low—4 cases	10, 17, 26, and 48 hours

Such figures emphasize not only the great severity of strangulation as compared with simple obstruction, but also the fact that when the gut is strangulated there is no evidence that a lesion high in the small intestine is more rapidly fatal than one situated at a lower level. From the figures given above Murphy and Vincent concluded, therefore, that blockage of the venous return was the most important factor in the production of this rapid intoxication. They were able to show that venous occlusion produced marked destructive changes in the gut mucosa within a period of four to five hours, such changes being absent in total anæmia. In their view death was due to the absorption through the damaged mucosa of bacterial toxins from the gut lumen, which entered the circulation through the lymphatic system.

Much has been written of bacterial toxins in relation to acute intestinal obstruction, especially those of the *Bacillus welchii*. The work of McIver, White, and Lawson[39] at least disposes of the *B. welchii* group. Working with cats they prepared 20-cm. strangulated loops by individual ligation of the mesenteric veins. Such animals had a survival period of eighteen to thirty-two hours. The investigation showed that the *B. welchii* present in the loop were mostly of an avirulent strain, that cats immune to *B. welchii* toxin succumb rapidly to strangulation, and that there was no evidence that life could be prolonged by the administration of antitoxin. Death occurred before there had been more than a slight fall in the blood-chloride content. It appears that in intestinal strangulation we can attribute death neither to *B. welchii* toxæmia nor to hypochloræmia.

Foster and Hausler[40] attribute death to different causes according to the length of the gut involved. They produced strangulation of various lengths of intestine in dogs by a rubber ligature surrounding the mesentery, and found that the survival was inversely proportional to the length of loop affected.

5-in. segment—survival 29 hours
15-in. segment—survival 22 hours
26-in. segment—survival 8·5 hours, etc.

They attribute death in animals with long-loop strangulation to shock—the result of distension and violent peristalsis together with loss of fluid from the circulation into the strangulated segment. When a short loop was affected the initial shock

was insufficient to account for death, which resulted later from the absorption of toxins, believed by them to be of bacterial origin, from the peritoneal cavity. By enclosing the strangulated segment in a rubber bag they were able to prevent this absorption into the circulation and to prolong life. They again point out that hypochloræmia cannot be a lethal factor in strangulation, as death takes place in the presence of almost normal blood-chlorides. Holt,[41] in repeating this work, came to similar conclusions, and in particular laid emphasis on the fact that death in long-loop strangulation was due entirely to the fluid loss. In medium loops he agrees with the conclusions of Foster and Hausler given above, except that the toxin is produced by bacterial proteolytic action on the gut wall and is not derived directly from the content. Although his loops were prepared by individual ligature of mesenteric veins, the significance of which will be pointed out later, he regards the route of absorption of this toxin as being via the peritoneal cavity in the latter stages. In very short loops he attributes death either to peritonitis, the result of perforation aided by the exudation of toxic loop content, or, in the case of femoral hernia, which he regards as extraperitoneal, as due simply to the obstruction and its resulting dehydration. The toxic properties of the peritoneal fluid seen in the latter stages are attributed by him to the presence of a proteose.

EXPERIMENTAL METHODS AND RESULTS

Our investigation was taken up with the object of determining the relative importance of fluid loss and toxæmia in producing the circulatory collapse of intestinal strangulation in loops of all sizes, as it seemed to us improbable that a toxin, whatever its source, which eventually appeared in the peritoneal fluid, could be without significance before its arrival at this point, and might therefore contribute to the collapse even in long-loop strangulation. We have been led from this initial point to an investigation of the source, the absorption, and the excretion of the toxin, a study of its action, and the possible effects resulting from its absorption following the relief of a strangulated segment. The details of the various operative procedures will be given under their appropriate sections, but certain general considerations must be dealt with at this point.

Since, as already indicated, there seems little ground for believing that the toxicity of strangulated loops varies with the level of the lesion, we have made a practice of forming our short strangulated segments at approximately the middle of the small intestine. It became necessary in the course of the investigation to be able to form strangulations of greater or lesser severity. Two procedures were adopted to this end.

1. **Severe Strangulation : Non-viable Type.**—The length of small intestine to be strangulated was carefully measured, and obstructing ligatures were placed around the gut at the limits of the selected length, producing a closed loop. The marginal vein at the gut border was ligatured and the individual veins in the mesentery draining the affected segment were tied off, leaving the arteries patent. The gut in the affected segment was thus in a condition of extreme venous strangulation, but since the mesentery was not compressed, *the lymphatics leading from it were not occluded.* Such a segment gradually became cyanosed and the mesentery engorged. Within a period of twenty-four hours the gut lost its 'viability', although no actual gangrene was present. The lumen was in all cases distended

with dark hæmorrhagic fluid. Sometimes a few of the mesenteric veins were thrombosed. The peritoneal fluid was copious, markedly blood-stained, and possessed a characteristic odour. From the dark colour of the gut such loops are referred to in this paper as 'black loops' (*Fig.* 594).

2. Mild Strangulation: Viable Type.—A length of loop was again measured, and obstructing ligatures were tied lightly so as to compress the gut without cutting into the wall, threads being left long in order to anchor the rubber ligature. The gut and mesentery were then surrounded with a rubber band. The tension on this was adjusted until the veins appeared perceptibly full and there was slight congestion of the mesentery and bowel; the ends of the band were then stitched together. Such compression of course affected the lymphatics of the mesentery as well as the veins. The gut gradually became dark pink in colour, and retained its 'viability' at the end of twenty-four hours. In these cases, also, the lumen was markedly distended by fluid. Peritoneal fluid was copious, clear, and odourless. From the colour of the gut such loops are referred to as 'pink loops' (*Fig.* 595). In a few cases where the tension on the ligature had been too great, the character of the gut and peritoneal fluid at twenty-four hours approximated to the condition of the former non-viable group. In all survival cases the operations were conducted with full aseptic technique and ether anæsthesia was employed.

EXPERIMENTAL RESULTS

SURVIVAL TIMES

In our early results we were able to confirm the findings of Murphy and Vincent[38] on the contrast between simple obstruction, venous strangulation, and total anæmia. As controls single-ligature obstructions and simple closed-loop obstructions of the same length as the strangulated segments were used (*Table IV*).

Table IV

LESION	POSITION	SURVIVAL TIME	REMARKS
Simple obstruction ..	Middle small intestine	Hours 240 approx.	Peritonitis at ligature, no vomiting
Closed loop 20 cm.	Middle small intestine	163	Post mortem—peritoneum clear. No distension of loop (vomiting marked)
Total anæmia 20 cm.	Middle small intestine	48	Gangrene, peritonitis. No fluid loss
Strangulation (black loop) 20 cm.	Middle small intestine	19	Peritoneal exudate as described, no infection

Comparison of the survival times of two series of strangulated segments of moderate length but different degrees of severity, prepared by the methods that have already been indicated, shows a marked difference of the survival period (*Table V*).

Fig 594—Non-viable strangulation of 24 hours' duration
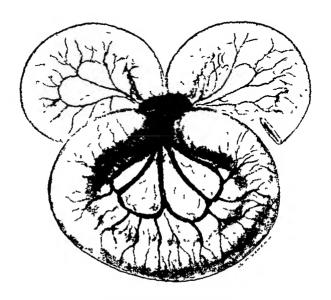
Fig 595—Viable strangulation, 24 hours' duration

Table V

	WEIGHT	LENGTH OF LOOP	SURVIVAL TIME
	Kg.	Cm.	Hours
Series I : Black Loops.—			
1	2·25	17	45
2	2·5	17	20·5
3	2·75	17	20
4	3·75	17	36
5	2·5	32	18
6	3·0	35	12
7	2·75	40	21
Series II : Pink Loops.—			
1	1·75	17	82
2	2·25	17	B.P. 110 at 22 hrs.
3	2·5	17	B.P. 70 at 22 hrs.
4	2·5	17	B.P. 100 at 48 hrs.
5	2·5	17	B.P. 100 at 48 hrs.
6	2·5	17	B.P. 110 at 48 hrs.
7	2·5	17	B.P. 60 at 48 hrs.
8	2·75	17	B.P. 70 at 22 hrs.
9	3·0	17	B.P. 110 at 48 hrs.
10	3·0	32	B.P. 90 at 20 hrs.

Since there is so marked a difference in the survival time where venous strangulation is present, it is well to consider its physiological consequences, for amongst them must be factors which accelerate the fatal outcome. They are obviously :—

1. Stagnation of blood in the local area.

2. Raised capillary pressure, resulting in increased tissue fluid formation and exudation into the bowel lumen and peritoneal cavity.

3. Distension of the gut.

4. Increased lymphatic fluid production with increased opportunities for absorption (provided the lymphatics are not compressed).

5. Stagnation anoxæmia and consequent changes in tissue metabolism progressing to devitalization of tissue.

The first two of these lead to loss of fluid from the circulation. The last two are of importance in relation to toxæmia.

THE FLUID-LOSS FACTOR

Medium-length Loops.—As well as the survival time the fluid loss occurring was also noted in order to estimate the significance of this factor as a cause of death. The following method was adopted : The length of the segment to be strangulated was accurately measured at operation. At post-mortem the peritoneal cavity and intestines were swabbed dry with wool swabs of a known weight, which were then weighed. The strangulated segment was excised together with its mesentery, and weighed. From the figure obtained by the addition of these two weighings was subtracted the weight of the wool and the weight of a section of

normal intestine and mesentery from the same animal of a length equal to the original segment. The difference in weight is accounted for by peritoneal exudate, fluid in the gut wall and mesentery, and extravasated fluid in the lumen. The importance of measuring a length of intestine equal to that which was taken *before* strangulation is that a great increase in size results from the distension. Foster and Hausler put this increase as high as two to three times the original length. In our experiments the average increase was just under one-third of the original length. The weight obtained for the total fluid loss is expressed as a percentage of the body weight of the animal (*Table VI*).

Table VI

	WEIGHT	LENGTH OF LOOP	SURVIVAL TIME	FLUID LOSS BODY WEIGHT	PER CENT BODY WEIGHT
	Grm.	Cm.	Hours		
Series III : **Black Loops.—**					
1	2250	17	45	$\frac{27}{2250}$	1·2
2	2250	17	21	$\frac{36}{2250}$	1·6
3	2750	17	20½	$\frac{43·5}{2750}$	1·7
4	2750	17	20	$\frac{34}{2750}$	1·2
5	3000	17	36	$\frac{22}{3000}$	0·7
6	3750	17	36	$\frac{50}{3750}$	1·33
7	2250	32	18	$\frac{31}{2250}$	1·5
8	3000	35	12	$\frac{78}{3000}$	2·6
9	2750	40	18	$\frac{102·5}{2750}$	3·7
Series III : **Pink Loops.—**					
10	2500	17	75	$\frac{22·5}{2500}$	0·9
11	1750	17	82	$\frac{35}{1750}$	2·0
12	2750	17	48	$\frac{12}{2950}$	0·44

These figures show conclusively that there is no constant relationship between the amount of fluid lost from the circulation and the survival period, nor does the difference in fluid loss account for the varying survival times seen in *Series I* and *II*. In *Series III*, No. 5, a black loop with fluid loss of 0·7 per cent body weight survives 36 hours. No. 10 in the same series shows a pink loop of equal length with fluid loss 0·9 per cent body weight surviving 75 hours. No. 11, a pink loop, with fluid loss 2 per cent survives 82 hours, whereas Nos. 1 to 4, black loops of equal length having a fluid loss from 1·2 to 1·7 per cent, survive from 20 to 45 hours. In certain cases those animals showing the larger fluid loss survive for a shorter period, though there are obvious exceptions to this. In no case is the volume of fluid loss sufficient to account for death. Blalock[45] has shown that it is necessary to remove amounts of blood representing at least 4 per cent of the body

weight in order to produce death from fluid loss alone. Removal of 2 to 3 per cent gives rise to tachycardia and slight stupor, and only a mild degree of shock. We have repeatedly confirmed this observation. Fluid loss, therefore, plays at most only an accessory rôle in the production of circulatory collapse resulting from medium loop strangulation.

FIG 596 —Carotid blood-pressure record showing effect of strangulation of entire small intestine of cat Survival time: 2 hours Fluid loss: 2 2 per cent of body weight. Sig 1, Abdomen opened , Sig 2, Ligature of veins , Sig. 3, Ligature of intestine.

Long-loop Strangulation.—Holt[41] has stated that in long-loop strangulation " there is no evidence of any toxæmic process, and death is due solely to the withholding of a large volume of blood from the circulation by the loop." To examine this point continuous blood-pressure records were made of cats anæsthetized with chloralose. The intestine was exposed and ligatures tied around the upper duodenum, and the ascending colon above the right colic vein. All collateral veins
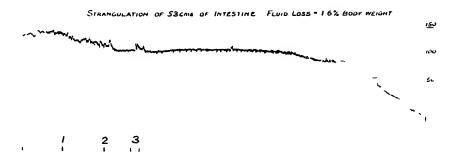
FIG 597.—Carotid blood-pressure record showing the effect of strangulation of 53 cm of small intestine. Survival time : 1 hour 10 minutes Fluid loss · 1·6 per cent of body weight Sig. 1, Ligature of mesenteric veins ; Sig. 2, Ligature of collateral veins , Sig. 3, Ligature of intestine.

having been ligatured at these levels, the superior mesenteric vein was then tied below the junction with the splenic vein. A mass strangulation of the whole small intestine and portion of the upper colon was thus produced. This method will subsequently be referred to as ' superior mesenteric strangulation ', and represents an extreme degree of long-loop strangulation.

Typical blood-pressure records obtained under these conditions are shown in *Figs.* 596, 597. At the end of the experiment the fluid loss was determined, by the following method. The peritoneal exudate was assessed in the manner stated above (p. 829), then the gut and mesentery were excised between the ligatures. The gut content, usually a few cubic centimetres of thick muco-hæmorrhagic fluid, was expressed and weighed. The gut and mesentery were then weighed. The total length of the intestine was then measured. After due allowance had been made for distension, the length obtained was multiplied by a weight factor derived from the examination of a series of 10-cm. lengths of normal small intestine. The weight so obtained was subtracted from the total weight of peritoneal fluid, gut content, strangulated wall and mesentery, and the figure for the fluid loss obtained (*Table VII*).

Table VII

	WEIGHT	LENGTH OF INTESTINE	SURVIVAL TIME	FLUID LOSS	PER CENT OF BODY WEIGHT
Series IV.—					
	Kg.	Cm.	Hours		
1	1·75	80	2	$\frac{39}{1750}$	2·2
2	1·5	53	—	$\frac{24}{1500}$	1·6
3	3·0	25	Killed at 7½ hours B.P. 30 mm.	$\frac{42}{3000}$	1·4
4	3·8	107	2¾	$\frac{64}{3500}$	1·8

It will be seen that here again the figure obtained for the fluid loss is in no case adequate to account for death even in the longest loops. The largest loss, that of 2·2 per cent, when produced by a rapid hæmorrhage, will cause an initial fall of pressure as shown in *Fig.* 596, which is the tracing taken from this animal, but hæmorrhage alone, as we have repeatedly found, is followed by a rapid recovery in the blood-pressure to a slightly lower level than the previous normal (*see Fig.* 600B), and is not succeeded by the gradual decline in pressure terminating in death as shown in this tracing. While admitting that the initial fall of pressure seen in certain cases can be due to fluid loss, we could not on this evidence admit that the fatal outcome was due to this factor alone. In view, however, of Holt's statement further experiments were conducted to settle this point.

Cross-circulation Experiments.—Two animals of approximately equal weight were selected. In one superior mesenteric strangulation was prepared by the method described above, a ligature being placed on the superior mesenteric vein but left untied. The carotid artery of the second animal was then connected through a Payr's cannula to the superior mesenteric artery supplying the segment to be strangulated, forming with it a surface lined completely with intima. The superior mesenteric vein was then tied and the clip removed from the carotid artery. The blood then flowed into the gut, which soon presented all the features of strangulation. Blood-pressure records were taken from the femoral artery of the supplying animal and the carotid artery of the recipient.

The blood-pressure of the 'supplying' animal shown in *Fig.* 598 remained steady despite the fact that it was suffering the entire fluid loss, which was subsequently estimated as 1·6 per cent of its body weight, a figure which corresponds well with those shown in *Table VII.* The 'strangulated' animal showed a progressive decline in blood-pressure comparable to that seen in *Fig.* 596, and died in one and a quarter hours, despite the absence of fluid loss. It will be noted that there is no rapid initial fall as shown in *Fig.* 596, which we have attributed to the
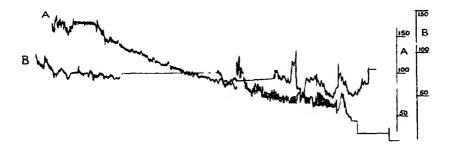
FIG. 598.—Cross-circulation experiment : Cat B supplying blood to strangulated intestine of Cat A. Death of strangulated Cat A in 1¼ hours despite absence of fluid loss.

loss of fluid. The significant feature is, however, the gradual decline in pressure which is maintained from the commencement of the strangulation.

Another similar experiment (*Fig.* 599) shows the supplying animal remaining at a steady pressure despite a fluid loss of 1·4 per cent of the body weight. The strangulated animal at first maintains its initial blood-pressure, later showing a progressive decline to death comparable to that seen in *Fig.* 597, despite the absence of fluid loss.
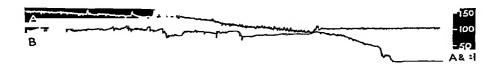
FIG. 599.—Cross-circulation experiment : Strangulated animal A dies after 2 hours. Fluid loss: 1·4 per cent of body weight of Cat B.

The experiment depicted in *Fig.* 600 is similar, but in addition illustrates the effect on blood-pressure of a large and rapid fluid loss, in this case amounting to 3·3 per cent of the body weight of the supplying animal. It will be seen that the initial fall of blood-pressure in the supplying animal is not followed by any progressive decline in pressure, the animal still showing a pressure of 90 mm. when the strangulated animal died.

These experiments prove conclusively that in long-loop strangulation death cannot be due to fluid loss alone. We therefore hold that whatever the length

of the loop affected, fluid loss plays no more than an accessory rôle in the production of the circulatory collapse of intestinal strangulation. The fatal result is in the main due to some other more important factor—either chemical or nervous.

In this paper we are concerned only with the chemical agency, consideration of a possible nervous mechanism being deferred.
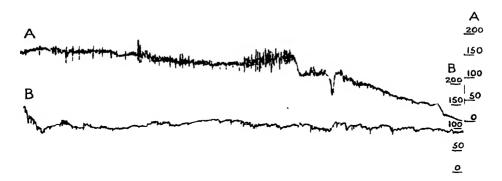
FIG. 600.—Cross-circulation experiment : Cat B (lower tracing) supplying blood to strangulated small intestine of Cat A (upper tracing). Death of Cat A after 2¾ hours. Fluid loss : 3·3 per cent of body weight of Cat B.

THE TOXIC FACTOR

Toxic Factor in the Peritoneal Fluid.—In order to confirm the toxicity of peritoneal fluid in the latter stages of strangulation of the black-loop type, and observe the result of its absorption from the peritoneal cavity, the following experiment was performed : A black loop of 17 cm. was formed and encased in a rubber bag. After 16½ hours the abdomen was opened and the 45 c.c. of fluid contained

FIG. 601.—Effect of absorption of peritoneal fluid. Cat A (lower tracing), strangulated 16½ hours previously. Cat B (upper tracing), normal animal. Sig. 1, Peritoneal fluid and strangulated intestine of Cat A transferred to peritoneal cavity of Cat B ; Sig. 2, Death of Cat B 3½ hours later ; Sig. 3, Death of Cat A 20½ hours after original strangulation.

in the bag together with the loop were placed inside the peritoneal cavity of a normal animal. The abdominal walls of the two animals were sutured together and continuous blood records taken from each under chloralose anæsthesia (*Fig.* 601). The normal animal died in 3½ hours, having absorbed 30 c.c. of the exudate. The strangulated animal died shortly after, in a period of 20½ hours. This shows that the toxin appearing in the peritoneal fluid in cases of the non-viable type can

by itself without any fluid loss produce circulatory collapse and death in a normal animal.

Intravenous injections into the normal animal of peritoneal fluid derived from survival cases of the non-viable type, with one doubtful exception, always depressed
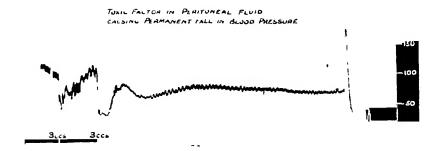
FIG. 602.—Peritoneal fluid. Depressor effect on blood-pressure of normal cat of intravenous injection of peritoneal fluid from a non-viable strangulation of 24 hours' duration. Sig. 1, 3 c.c. peritoneal fluid intravenously; Sig. 2, 3 c.c. peritoneal fluid intravenously.

the blood-pressure, provided the fluid was obtained a sufficient interval after the onset of strangulation. Following the initial fall in blood-pressure, the further character of the tracing varies. With small doses the blood-pressure usually returns to its original level. With larger doses the initial recovery does not take place,
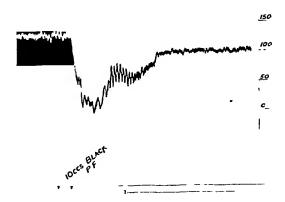
FIG. 603.—Peritoneal fluid. Depressor effect of intravenous injection into a normal cat of 10 c.c. peritoneal fluid from a non-viable strangulation of 23 hours' duration.

but instead the pressure returns slowly and remains stable at a permanently lower level. These reactions are illustrated in *Fig.* 602.
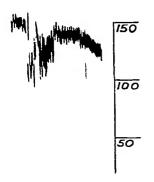
During the recovery phase the pulse was frequently observed to be slow and irregular. The presence of numerous dropped beats suggested that the toxic substance had some effect on the heart's action. (*Fig.* 603—*see also Fig.* 604.)

The permanent lowering of blood-pressure is of great significance in view of its relation to the clinical picture of intestinal strangulation.

Table VIII

VOLUME	FRESH OR POST-MORTEM	SITE OF INJECTION	EFFECT	DURATION OF STRANGULATION
c.c.				Hours
Series V: **Viable Loops.—**				
60	Fresh	Intraperitoneal	Not toxic	22
20	Fresh	Intravenous	Not toxic	21
6	Fresh	Intravenous	Not toxic	48
6	Fresh	Intravenous	Pressor	48
2	Fresh	Intravenous	Pressor	29
10	Fresh	Intravenous	Pressor	23
2	Fresh	Intravenous	Pressor	24
Series V: **Non-viable Type.—**				
37	Fresh	Intraperitoneal	Death 3½ hours	16½
1	½ hr. P.M.	Intravenous	Depressor	12
1	12 hr. P.M.	Intravenous	Depressor	36
2	Fresh	Intravenous	Pressor ? ?	30
3	Fresh	Intravenous	Marked depressor	24
1	Fresh	Intravenous	Marked depressor	29
3	Fresh	Intravenous	Marked depressor	20
2	Fresh	Intravenous	Slightly depressor	20

A similar series of experiments using peritoneal fluid from ' viable ' or ' pink ' loops shows that there is no evidence of a toxic substance in such fluid. The intraperitoneal injection into a normal cat of 60 c.c. of peritoneal fluid collected in a rubber bag surrounding a ' viable ' loop twenty-two hours after strangulation produced only a slight rise in blood-pressure. Intravenous injections of similar fluids (*see Figs*. 606, 619) are either without effect or give a mild pressor response. The difference in these results is shown in *Table VIII*.

It is obvious, therefore, that a toxic substance appears in the peritoneal fluid within twelve hours of strangulation of the black-loop type, but that in the pink-loop type even after forty-eight hours of strangulation the peritoneal fluid has normal physiological effects, i.e., it is non-toxic.

We have investigated the time at which the depressor substance can first be recognized in peritoneal fluid. It can be demonstrated within sixty to seventy minutes of the production of a superior mesenteric strangulation. The fact that the peritoneal fluid in ' viable ' loops does not contain a toxic substance within the time at which its presence can always be demonstrated in non-viable loops may explain the longer survival period already noted in

IO CCS PINK FLUID.

FIG. 604.—Peritoneal fluid. Slight depressor effect of intravenous injection into a normal cat of peritoneal fluid from a loop with doubtful viability of 24 hours' duration.

milder strangulations. A further point in the relationship between the toxicity of the exudate and the severity of the strangulation is brought out by the following observation : In two cases an attempt had been made to form viable loops, but,
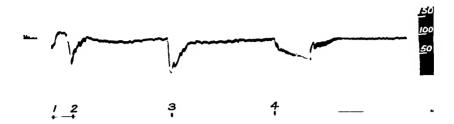
FIG 605 —Effect of injection of peritoneal fluid and blood from the mesenteric veins of a non-viable strangulation Sig 1, Intravenous injection of 4 c c of peritoneal fluid , Sig 2, Intravenous injection of 5 c.c of peritoneal fluid, Sig 3, Intravenous injection of 1 c c of mesenteric venous blood, Sig 4, Intravenous injection of 9 c c of peritoneal fluid.

owing to excessive tension on the ligature, border-line cases of rather more severe strangulation and doubtful viability were produced at twenty-four hours.

The peritoneal fluid in these cases was slightly tinged with blood and gave a mild depressor reaction (*Fig.* 604). The severity of the strangulation, therefore, governs the time of appearance of a depressor substance in the peritoneal fluid.

Toxic Factor in the Gut Blood. —Viable and non-viable segments were constructed and after approximately twenty hours the abdomen was opened under anæsthesia and the blood in the mesenteric veins draining the loops aspirated and injected intravenously into normal animals. Injections of peritoneal fluid from the same cases were also made and the effects contrasted.

Fig. 605 shows the results obtained by this method with material taken from a 17-cm. non-viable loop at twenty hours. A similar depressor substance is present both in the gut blood and in the peritoneal fluid. The injection of 1 c.c. of blood (Sig. 3) produces the same effect as the injection of 5 c.c. of peritoneal fluid (Sig. 2), suggesting a greater concentration in the former. The abnormal cardiac activity that

FIG 606 —Effect of injection of peritoneal fluid and mesenteric venous blood from a viable strangulation of 17 cm small intestine of 22 hours' duration Sig 1, Intravenous injection of 1 c c of peritoneal fluid Sig 2, Intravenous injection of 1 c c of mesenteric venous blood , Sig 3, Intravenous injection of 1 c c of peritoneal fluid , Sig 4, Intravenous injection of 2 c c of mesenteric venous blood

has been already referred to is well shown during the recovery phase in this tracing (Sig. 4).

The injection of material derived from a viable loop at twenty-seven hours (*Fig.* 606) demonstrates that whereas the peritoneal fluid has a pressor reaction (Sigs. 1 and 3), as already described, the reaction of the gut blood in this case is

mildly depressor (Sigs. 2 and 4), though quantitatively less than in the case of non-viable gut (cf. *Fig.* 605, Sig. 3). A study of our results on this point shows that the gut blood always contains a markedly depressor substance in the case of non-viable loops, but that in viable loops the results are variable. The blood may contain either a smaller or equal amount of depressor substance in comparison with the blood of non-viable segments.
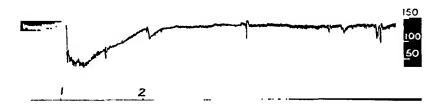
FIG. 607.—Effect of intravenous injection into normal cat of mesenteric venous blood from a very mild strangulation of 17 cm. of small intestine of 20 hours' duration. Sig. 1, Intravenous injection of 10 c.c. of mesenteric venous blood (anticoagulant—novhirudin); Sig. 2, Control injection of novhirudin solution.

Fig. 607 shows a case in which the blood from a very mild strangulation ('pink loop') after twenty hours contained a large amount of depressor substance. In one case of our series the gut blood of a viable loop at twenty-four hours gave a marked and pure pressor reaction ; the reason for this variability has not yet been determined.
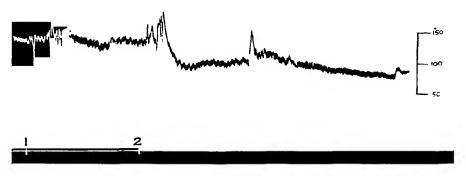
FIG. 608.—Blood collected from mesenteric veins after mass strangulation of small intestine for 1 hour and dialysed (10 c.c. dialysate equivalent to 1 c.c. of blood). Effect of injection of dialysate on blood-pressure of normal cat. Sig. 1, 10 c.c. of dialysate intravenously ; Sig. 2, 50 c.c. of dialysate intravenously.

Time of Appearance.—In order to determine the period required before the appearance of depressor substance in the blood, superior mesenteric strangulations were performed and blood was collected by cannulation of the superior mesenteric vein and tested by intravenous injection in a normal animal. The presence of depressor substance was demonstrated in the venous blood in from thirty minutes to one hour from the onset of strangulation. Examination shows that this depressor substance is readily dialysable through a semi-permeable membrane (*Fig.* 608).

In this experiment blood was collected from the mesenteric vein into a weak anticoagulant solution (novhirudin) after one hour's strangulation and dialysed against ten times its volume of normal saline for twenty-four hours. It will be seen that 50 c.c. of dialysate, the equivalent of 5 c.c. of blood, are markedly depressor (Sig. 2), the effect being even more striking when we consider that the administration of 50 c.c. of saline by intravenous injection should by itself cause a very marked rise in pressure. This tracing also shows that whereas a small dose of fluid containing toxic material produces an effect with rapid recovery of the blood-pressure to normal (Sig. 1), a larger dose causes the permanent depressor effect already referred to (Sig. 2). In the examination of mesenteric blood from other experiments it was noted sometimes that the substance present appeared to have a profound effect on the heart of the injected animal. Small doses caused a slight fall in blood-pressure, but any attempt to give a large dose led to the immediate death of the injected animal by ventricular fibrillation. At post-mortem the liver was found to be engorged with dark blood. (*Figs.* 609 and 622, Sig. 5). We have met this phenomenon in three cases in our series.

In view of the fact that Donomae and Feldberg,[46] in examining the portal blood of normal animals, had met with depressor effects in 3 out of 15 of their series, due to some substance other than acetylcholine, it was necessary to establish that the depressor substance observed in our cases had arisen as the direct result of strangulation. A superior mesenteric strangulation was prepared, the portal vein being exposed but left untied. A ligature was put in position above the point of junction of the splenic vein with the portal, and a cannula inserted into the splenic. Novhirudin was then administered to the animal and a sample of portal blood extracted from the splenic cannula.
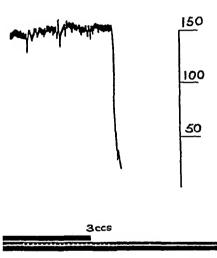
FIG. 609.—Injection of 3 c.c. of serum derived from venous blood from a strangulated segment of 20 cm. small intestine of 45 minutes' duration causes sudden death.

The portal vein was then tied and strangulation produced. After one hour's strangulation blood was again withdrawn from the portal vein. Intravenous injection of these samples into the normal animal showed that portal blood before strangulation gave a pressor reaction. The first sample removed after strangulation, which was merely the blood arrested at the upper end of the portal vein, was also pressor. The second sample which had been allowed to flow upwards from the gut was markedly depressor (*Fig.* 610). This result was constant in all five cases.

The character of the depressor effect seen in the tracings of different experiments showed variations, and in some cases alteration of the cardiac rhythm was noted. The question whether these differences are due to the presence of more than one substance or different concentrations of the same substance is under investigation. Our present results tend to support the latter view. It is definitely established, however, that a depressor substance appears in the venous blood within

thirty minutes to one hour from the onset of strangulation. The rapid appearance of the substance seems to rule out the possibility of a bacterial origin.

In order to determine whether the depressor substance is produced by the tissues of the gut wall by some abnormal process as the direct result of strangulation, or is merely a substance already existing in the lumen, which is absorbed under the new conditions, the following experiment was performed: The intestine was divided transversely immediately distal to the pylorus and above the ileocæcal valve. The pyloric and ileocæcal ends were ligatured and invaginated. Cannulæ were then tied in to the upper and lower ends of the isolated small intestine and connected to tubes through which the gut was irrigated. The lumen was washed through with 4 to 5 litres of warm water until the washings were quite clear. The water was then displaced with air and a variable quantity of warm normal saline introduced, usually 80 to 100 c.c. The rubber tubes were then clipped off, and by means of a water manometer connected through a side limb to the lowest cannula the pressure inside the lumen was recorded. After half an hour the saline was displaced and an equal volume of fresh saline introduced. The gut was then strangulated by ligature of the superior mesenteric vein and left for a further period of one hour, during which the pressure was noted. At the end of this time, the saline was again displaced from the lumen and a sample of blood removed from the mesenteric vein. Two samples of saline from the lumen were thus obtained, the first from normal resting intestine, the second from strangulated intestine. Each sample was filtered and the filtrate centrifuged. The first appeared clean, the second slightly blood-stained. These samples were then tested by intravenous injection in the normal animal. It was found in all cases that whereas the saline during the resting period was without any effect, the washing from the gut lumen was definitely depressor after one hour's strangulation. The samples of blood after one hour's strangulation were, with one exception, also depressor. These results may be seen from the *Table IX*.

FIG. 610.—Effect of intravenous injection into normal animal of portal blood before and after strangulation. Sig. 1, Intravenous injection of 2 c.c. of portal blood before strangulation; Sig. 2, Intravenous injection of 2 c.c. of portal blood 1 hour after strangulation.

It will be noted that in no case does any depressor substance appear in the gut lumen during the normal resting period, nor could its presence be demonstrated in a control experiment in which simple obstruction was substituted for the strangulated period. *Fig.* 611 also illustrates these results, and in addition shows that the substance present in the gut lumen sometimes affects respiration, producing apnœa. The presence of a similar substance in the filtrate from the gut content of a viable loop excised at 24 hours is illustrated in *Fig.* 612 (Sig. 1), which also shows the marked depressor content of the venous blood in the same case (Sig. 2). These results appear to show that the depressor substance arises in the wall of the gut itself and passes from there both into the lumen and into the venous blood. Since it is not present in the lumen before strangulation, and since the rapidity of its formation in high concentration appears to rule out a bacterial origin, it would

seem that the toxin arises from the tissues of the gut wall as the result of intrinsic changes consequent upon venous strangulation. Such an origin for the depressor substance is well within the bounds of physiological possibilities. It is known that extracts from the wall of the intestinal tract contain depressor substances other

Table IX

IRRIGATION	RESTING PERIOD, ½ HOUR		STRANGULATED PERIOD, 1 HOUR		GUT BLOOD 1 HOUR AFTER STRANGULATION
	Pressure	Content	Pressure	Content	
1	4 litres till clear	4 cm. water	Pressor 2 c.c.	10 cm. water	Depressor 2·5 c.c.	Marked depressor 2·5 c.c.
2	3 litres till clear	2 cm. water	Pressor 2 c.c.	7 cm. water	Depressor 2 c.c.	Pressor 2 c.c.
3	4 litres till clear	1 cm. water	No effect 2 c.c.	6 cm. water	Marked depressor 2 c.c.	Depressor 2 c.c.
4	5 litres till clear	1 cm. water	No effect 2 c.c.	10–16 cm.	Depressor 2 c.c.	Marked depressor 4 c.c.

than histamine and acetylcholine. According to Euler and Gaddum[47] the muscle of the intestine is the source of depressor substance which gives blood-pressure reactions very similar to those already described in our experiments. Lim, Ling, and Liu[48] have prepared from intestinal mucosa an extract, the depressor effects
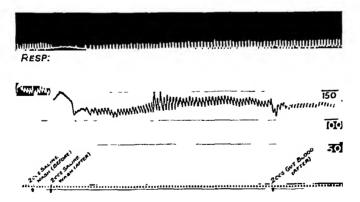
FIG. 611.—Effect of injection of intestinal contents before and after strangulation. Lumen of small intestine washed till clear. Filled with saline and left for half an hour. Saline removed and filtered; 2 c.c. of filtrate injected into test animal (Sig. 1). Intestine strangulated for 1 hour. Lumen of intestine washed with saline. Filtered. 2 c.c. of filtrate injected into test animal (Sig. 2); Sig. 3, 2 c.c. of portal blood 1 hour after strangulation.

of which are even more closely comparable to ours. This they believed to be a mixture of a small quantity of histamine with the Euler-Gaddum-Felix-Lange substance, and state definitely that its effects are not due to acetylcholine, adenyl compounds, kallikrein, or Major's non-guanidine depressor substance. We are not yet in a position to identify the substance or substances concerned in our reactions.

Distension.—It will be noted that in the period of strangulation in the above experiment the highest pressure produced varied between 14 and 16 cm. of water. This was purposely selected to accord with the pressures recorded in cases of intestinal obstruction in the human by Sperling and Wangensteen,[49] who demonstrated pressures of 14 to 18 cm. of *water* reaching a maximum of 30 cm. at the height of peristalsis.   It is felt that the pressures of 80 to 100 mm. of *mercury* used by Taylor and his co-workers in the experiments already referred to are somewhat excessive, although McIver, White, and Lawson[39] have demonstrated pressures of 54 mm. of mercury in the strangulated loops of cats.   That distension to a pressure of 80 to 100 mm. of mercury by itself produces significant results in the normal animal
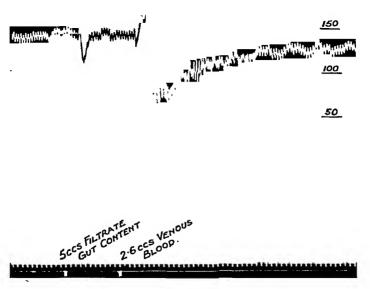
FIG. 612.—Effect of injection of filtrate of intestinal content and of venous blood from a 17-cm. viable loop of 24 hours' duration.   Sig. 1, 5 c.c. filtrate of gut contents ; Sig. 2, 2·6 c.c. mesenteric venous blood.

is undoubted.   The precise mechanism by which it does so is at present under investigation.   Our present results point to alteration in the degree of distension as the important factor rather than to simple distension at a constant pressure. This is of interest since peristalsis in the strangulated segment will obviously lead to rhythmic variations in pressure.

Distension in Normal Gut.—Fig. 613 shows the result of simple distension of a 17-cm. segment of normal gut to a pressure of 100 mm. of mercury.   During the period that the pressure is maintained there is a rise in blood-pressure which is due to a nervous mechanism and can be abolished by section of the sympathetic and vagus nerves.   Gradual relief of the distension is accompanied by a decline in blood-pressure to a lower level.   On further distension and relief the same effects are produced.   By this means the blood-pressure of a normal cat can be reduced to 90 mm. of mercury although death does not occur.   Whether this is due entirely

to a nervous mechanism or the local production of depressor substance is under investigation.

Distension with Venous Obstruction.—In certain cases we have found that simple venous occlusion from a short segment of intestine without obstructing ligatures around the lumen may be survived for a period of several days or indefinitely,
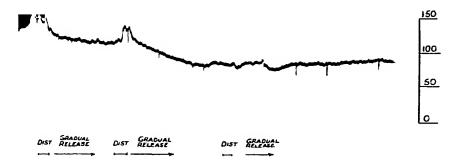
FIG. 613.—Effect on the blood-pressure of a normal animal of periodic distension of a segment of small intestine.

a partial venous collateral circulation being established. One animal had a blood-pressure of 120 mm. of mercury three days after such a procedure. On subsequent distension and relaxation of the affected segment a marked fall in blood-pressure and death resulted (*Fig.* 614). Rhythmic distension of the loop is, therefore, a factor of great importance. Whether its results are due to further production of the
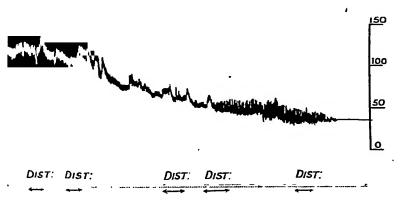
FIG. 614.—Effect on the blood-pressure of periodic distension of a segment of small intestine; following simple venous obstruction without occlusion of the lumen of the intestine performed 3 days previously.

depressor substance or to increased absorption from within the gut wall, or from the lumen, is at present under investigation. That increased lymphatic absorption of dye-stuffs results from distension of the intestine to 60 mm. of mercury pressure has already been demonstrated by Sperling and Wangensteen.[49] Absence of distension and diminished absorption may, therefore, allow the animal to survive

venous occlusion without obstruction, if the toxin is lost into the lumen. With a closed loop distension may promote absorption of depressor substance and hence allow it to produce its harmful effect. These conjectures, however, await confirmation. Distension is definitely an ancillary factor of great importance.

Absorption.—We have repeatedly observed at post-mortem that in every case where strangulation was produced by venous ligature alone, leaving the mesenteric lymphatics patent, as in superior mesenteric strangulation, and also in the formation of non-viable black loops, the large lymphatic channel in the mesenteric root and the thoracic duct have contained darkly-coloured or blood-stained fluid. A typical post-mortem appearance is illustrated in *Fig.* 615, which shows the condition of the thoracic duct in a superior mesenteric strangulation of two hours' duration.

FIG 615.—Photograph of thorax of cat showing the thoracic duct containing dark-coloured fluid 2 hours after superior mesenteric strangulation
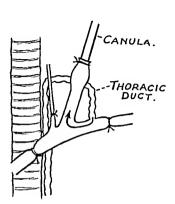
FIG 616.—Method adopted in order to study the changes in the thoracic-duct outflow consequent upon strangulation.

To study the changes occurring in the outflow from the thoracic duct consequent on strangulation a fistula was formed (*Fig.* 616). The duct was identified in the left side of the neck and traced to its entry into the veins. The subclavian, innominate, and internal jugular veins were ligated on either side of the point of entry of the thoracic duct, causing the chyle to flow upwards into the external jugular vein. By insertion of a cannula into this vein, variations in the duct outflow were noted. On the production of a superior mesenteric strangulation a considerable increase in the rate of flow occurred, followed after an interval of up to thirty minutes by a marked change of colour from the normal pearly white to red (*Fig.* 617). This change of colour is due to pigmented serum and not to cellular elements. Simple coloration of the fluid does not, however, indicate a recognizable toxicity; depressor substance appears in the duct in recognizable quantity somewhat later, in our series between forty to seventy minutes of the onset of strangulation. The reason for this variation was not determined, but may possibly be a question of concentration. The experiment shows that in all those cases where the mesenteric lymphatics are patent,

absorption of depressor substance may occur directly into the thoracic duct, and thence into the systemic circulation. When, however, the lymphatics were occluded by compression of the mesentery, as in the formation of viable loops, we were not able to demonstrate depressor substance in the thoracic duct unless it were also present in the peritoneal fluid. In the latter case absorption appeared to be secondary from the peritoneum and not by a direct route from the gut lymphatics to the thoracic duct. This relationship is illustrated by the following results :—

VIABLE LOOP	GUT BLOOD	PERITONEAL FLUID	THORACIC DUCT
18 hours	Depressor	Pressor	Negative
24 hours	Depressor	Pressor	Negative
BORDER-LINE			
24 hours	Depressor	Depressor	Depressor
23 hours	Depressor	Depressor	Depressor

In cases of the viable type, although the thoracic duct contains no depressor substance, the substance is present in the mesenteric lymphatics, being dammed

FIG. 617.—Photograph of fluid collected from thoracic-duct fistula showing the change occurring 15 minutes after the production of superior mesenteric strangulation.

back in them, and, on relief of the strangulation, appears in the thoracic duct (*see Fig. 619*).

In order to investigate the relationship of peritoneal absorption to the thoracic duct a few cubic centimetres of trypan blue were placed in the peritoneal cavity and seen to appear in the thoracic duct within twenty minutes. In view of the statement sometimes made that herniæ in which the neck of the sac is shut off should be regarded as extraperitoneal, a similar experiment was conducted. The tunica vaginalis was carefully dissected and firmly ligatured at the neck. Injection of trypan blue into the tunica led to the appearance of the dye in the thoracic duct within sixteen minutes.

Any toxic substance passing into the peritoneal cavity or hernial sac may, therefore, find its way into the general circulation via the thoracic duct. The possible routes of absorption in the various types of experiments conducted are summarized in *Table X.*

This table helps us to explain the longer survival period of the viable series already noted in *Series I* and *II*. Whereas at twenty-four hours the thoracic-duct fluid is non-toxic in viable-loop experiments, in the non-viable group it is profoundly depressor or toxic owing to continual mesenteric and peritoneal absorption. The importance of this factor may be judged from *Fig. 618*, which shows the effect of intravenous injection into the normal animal of 1·5 c.c. of thoracic-duct fluid obtained from a non-viable loop experiment in poor condition and with low blood-pressure

at twenty-three hours.   The relationship between the severity of the strangulation and the survival time is obvious.   The appearance of depressor substance in the peritoneal fluid, and hence its absorption through the thoracic duct, is governed by the severity of the strangulation.   This is well illustrated in the viable and border-line cases, which, from their mode of formation by mesenteric compression, correspond

Table X

	MESENTERIC LYMPHATICS	PERITONEAL FLUID	THORACIC-DUCT FLUID
Superior mesenteric strangulation	Patent, depressor	Depressor after 1 hour	Depressor 30–70 mins.
Black loops, non-viable—24 hours	Patent, depressor	Depressor	Marked depressor
Pink loops, viable—24 hours	Closed	Pressor	Normal
Border-line, i.e., of doubtful viability but produced by pink-loop method	Closed	Depressor	Depressor

most exactly to intestinal strangulation in the human patient.   It will also be seen that where a black non-viable loop, prepared by the method already described, is enclosed in a bag, as in Holt's repetition of Foster and Hausler's experiment, not only is peritoneal absorption prevented, but compression of the mesentery by the neck of the bag occludes the mesenteric lymphatics.   Such experiments, therefore, do not prove that absorption of toxin in these cases only occurs through the peritoneum, but that, provided toxic absorption is prevented by either the mesenteric or peritoneal route, life may be prolonged. We have repeated these experiments with variable results.   In all cases where life was prolonged the thoracic-duct fluid was non-toxic.   In the less successful cases the duct fluid contained toxic or depressor substances.

FIG. 618.—Thoracic-duct fluid.   Effect of injection of 1·5 c.c. of thoracic-duct fluid collected from a cat with a non-viable strangulation of 23 hours' duration.

Relief of Strangulation.—Although the absorption of depressor substance before relief of the strangulation is undoubtedly important, the action of that fraction which remains dammed up in the veins and lymphatics of the strangulated loop is not without significance.   On division of the mesenteric ligature in cases of the viable type depressor substance previously held up in strangulated veins and lymphatics is set free into the circulation.   The lymphatics transmit the depressor substance into the thoracic duct as shown in *Fig.* 619, which illustrates the result of injection into the normal animal of material derived from a very mild ' viable '

strangulation at eighteen hours. The thoracic-duct fluid of the strangulated animal contained no depressor substance before the relief of strangulation (Sig. 2), since the peritoneal fluid was non-toxic (Sig. 1) and the lymphatics were compressed. Immediately after the strangulation was relieved depressor substance appeared in the thoracic-duct fluid (Sig. 3).
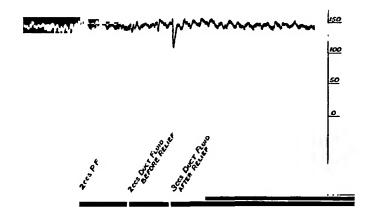
FIG. 619.—Thoracic-duct fluid. Relief of viable strangulation. Effect on the blood-pressure of a normal cat of intravenous injection of thoracic-duct fluid from another animal before and after relief of a viable strangulation. Sig. 1, Intravenous injection of 2 c.c. of peritoneal fluid; Sig. 2, Intravenous injection of 2 c.c. of thoracic-duct fluid before relief of strangulation; Sig. 3, Intravenous injection of 2 c.c. of thoracic-duct fluid after relief of strangulation.

When examining the fluid-loss factor we were repeatedly struck by the fact that relief of the venous obstruction, allowing the return of blood to the circulation, instead of improving the animal's condition always caused a further fall in blood-pressure. This, which would be inexplicable on the basis of the fluid-loss theory, is readily interpreted in relation to depressor substance in the veins. Such an experiment is illustrated in *Fig.* 620, where, following the relief of a very mild

FIG. 620.—Relief of strangulation. Decline of blood-pressure following relief of a viable strangulation of 17 cm. of small intestine of 26 hours' duration. Sig. 1, Relief of strangulation.

17-cm. viable strangulation at twenty-six hours, there is a progressive decline in blood-pressure from 120 to 60 mm. mercury in two hours.

Examination of the blood leaving a strangulated loop after relief of the strangulation shows that it continues to give a depressor reaction for thirty minutes or more, following relief of strangulation.

We believe that such re-absorption of depressor substance into the circulation accounts for the striking collapse shown in *Fig.* 621, where, following the relief of

a viable 17-cm. strangulation at twenty-two hours, the blood-pressure showed a rapid decline, and, despite the administration of saline and adrenalin, the animal died one and a quarter hours after the relief of strangulation.
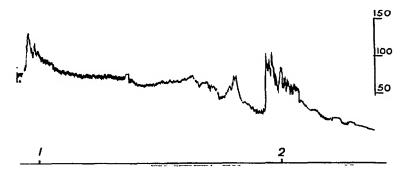
FIG. 621.—Relief of strangulation. Circulatory collapse following relief of viable strangulation of 17 cm. of small intestine of 22 hours' duration. Death of animal 1¼ hours later. Sig. 1, Relief of strangulation; Sig. 2, Intravenous adrenalin and saline.

Although evidence for the absorption of toxic material has been advanced, we have been unable to demonstrate the presence of depressor substance either in the carotid or heart blood of animals dying of experimental strangulation, nor could its presence be demonstrated in animals in which intravenous injections of toxic material had been performed. Whether this was due to rapid fixation or detoxication in the tissues, or rapid excretion from the body, is still the subject of investigation, together with the precise pharmacodynamic action of the substance on the heart and circulation. We have noted, however, that at post-mortem the liver frequently presents a nutmeg appearance, and a section shows evidence of fatty degeneration. Congestion of the renal glomeruli and fatty changes in the renal tubules have also been observed. Bearing in mind the demonstration of blood-pressure-reducing substances in the human urine by Adolf Bauer[50] and the work of Abelous and Bardier[51] on urohypotensine (see below), we were led to examine the urine of strangulated cats, in search of evidence of excretion of depressor substance.

FIG. 622.—Showing the effect of injection into a test animal of material derived from superior mesenteric strangulation experiment. Sig. 1, 2 c.c. plasma after 1 hour; Sig. 3, 0·5 c.c. urine after 1 hour; Sig. 4, 2 c.c. peritoneal fluid after 1 hour; Sig. 5, 2 c.c. blood after 2 hours; Sig. 2, 2 c.c. dialysate from urine of another cat with non-viable strangulation of 21 hours' duration.

It was found that 5 c.c. of urine from a cat with superior mesenteric strangulation of one hour's duration was markedly depressor (Fig. 622, Sig. 3), as were also the gut blood (Sig. 1) and peritoneal fluid (Sig. 4) from the same case. Two c.c. of the urine from an animal with

a non-viable black loop at twenty and a half hours was dialysed against normal saline; 2 c.c. of this dialysate also gave a depressor reaction (*Fig.* 622, Sig. 2). This tracing also shows the cardiac death produced by the injection of 3 c.c. of blood after two hours' strangulation (Sig. 5). Following the injection of depressor substance into normal cats we found that the urine of the injected animal gave a depressor reaction, whereas normal urine was pressor. The identification of this substance in the urine is proceeding. It is significant that it is readily dialysable, as has already been demonstrated in the case of depressor substance elsewhere. It is not present in the urine before strangulation, nor can it be demonstrated in appreciable amount in normal animals before the intravenous injection of depressor substance. We are therefore tempted to regard it as an excretion.

HUMAN MATERIAL

Some preliminary investigations have been conducted on material obtained from human cases of intestinal strangulation. In 3 instances in which a sample of peritoneal fluid was obtained no marked depressor effect was observed. In these cases the gut was viable and the strangulation of short duration. In 5 cases the urine was also examined with a view to determining whether excretion of a depressor substance had occurred. As mentioned previously, Abelous and Bardier[51] identified the existence of two components in normal urine. One component present in large amounts produces a marked pressor effect, so that the injections of small quantities of normal urine intravenously raise the blood-pressure, thereby masking the effects of a second component normally present in very small quantities, which, when extracted from large volumes of concentrated urine, has a depressor action. Bauer[50] showed that a blood-pressure-reducing principle present in very small amounts in normal urine was capable of being dialysed, and differed significantly in its properties from acetylcholine, adenylic acid, and histamine. He suggested that it possibly corresponded with the depressor substance not yet chemically defined which Euler and Gaddum had extracted from various tissues, including especially the smooth muscles of the intestinal wall. The similarity of these characteristics to those already noted in the case of depressor substance arising in the bowel wall, attracted our attention. It seemed justifiable to investigate the possibility that, under conditions of venous strangulation of the intestine, an increased amount of this depressor substance might be released into the circulation and give rise to an increased concentration in the urine. We have investigated the effects of urine from 5 cases of intestinal strangulation. In all of these a marked depressor effect was demonstrable on injecting a few cubic centimetres of urine. In such small doses urine from normal individuals was without effect on the blood-pressure, or alternatively produced a slight pressor reaction. The depressor substance was found to be readily dialysable. (*Fig.* 623.)

This tracing illustrates the injection of small quantities of the dialysate prepared from the urine of a patient with a viable strangulation of five hours' duration involving 18 in. of small intestine. In contrast to the similar dialysate from normal human urine which is faintly pressor, a marked depressor reaction is seen in the samples both before and after operation. It will be noted that the depressor effect is not precisely comparable in the samples before and after operation. This difference has been constant in all specimens examined, and may be due to differences

in concentration. In one case we have shown that this depressor effect, present at the time of operation, was no longer demonstrable on the seventh post-operative day. This fact, therefore, would seem to substantiate the hypothesis that the
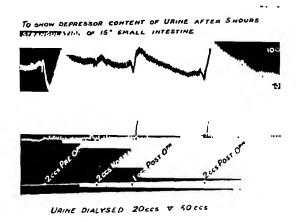
FIG. 623.—Effect of injection of dialysate of urine from human case of intestinal strangulation. Urine dialysed 20 c.c. v. 50 c.c. Sig. 1, 2 c.c. dialysate before relief of strangulation; Sig. 2, 2 c.c. dialysate of normal human urine; Sig. 3, 1 c.c. dialysate of urine after operation; Sig. 4, 2 c.c. dialysate of urine after operation.

appearance of this principle in marked concentration in the urine is definitely related to the occurrence of strangulation of the intestine. Our preliminary results are summarized in *Table XI*.

Table XI

CASE	NATURE OF STRANGULATION	EFFECT ON BLOOD-PRESSURE	
		Urine	Peritoneal Fluid
1	Femoral hernia—8-in. strangulation, 1 in. doubtful viability. Invaginated, died	Marked depressor ..	Not tested
2	Femoral hernia—5 in. viable small intestine	Not tested	Pressor
3	Femoral hernia—18 in. viable small intestine	Depressor before and after operation	Not tested
4	Internal band strangulation—12 in. viable small intestine	After operation depressor	Pressor ?
5	Inguinal hernia—knuckle of viable gut	Before and after operation depressor—7th day no effect	Pressor

DISCUSSION

From the introductory survey it will be seen that in order to account for the early onset of circulatory collapse which is so marked a feature of severe cases of intestinal strangulation and differentiates this condition from simple obstruction,

a mechanism which is capable of acting shortly after the onset must be sought. It has been shown that owing to their long latency, the factors disclosed by research into simple obstruction are inadequate in this respect, although they may be contributory in the later stages. Hypochloræmia alone can play no part in producing death, since death takes place in the presence of almost normal blood-chlorides. Loss of circulating fluid has been shown to play no more than an accessory rôle, whatever the length of the loop involved. There remain nervous or chemical factors. With the former we do not attempt to deal in this paper. With regard to the latter, in severe strangulation a depressor substance has been demonstrated in the wall of the intestinal tract within thirty minutes to one hour of the onset of venous obstruction and appears in the peritoneal fluid within one hour and in the thoracic duct within forty to seventy minutes. The first condition which any lethal factor must fulfil in order to account for the rapid collapse seen in severe cases, that of potential rapidity of action, is, therefore, satisfied. The second is that it should be capable of producing in the normal animal effects similar to those seen in the animal whose gut has been strangulated. In this early report of our first year's investigation we cannot advance complete evidence on this point. The pharmacodynamic action of the substance and the precise effects of continued slow absorption either alone or together with ancillary factors is the subject of further research. It has been shown, however, that the peritoneal absorption of 35 c.c. of the exudate from a black loop at sixteen and a half hours fulfilled this condition by causing death within three and a half hours in the normal animal. Since there is such complete similarity between the reactions of depressor substance in peritoneal fluid, gut blood, and elsewhere, it may be inferred that its slow continuous absorption from any site will produce a similar effect. That repeated or large doses do produce a permanent depression of blood-pressure comparable with the clinical picture of strangulation is a characteristic of all our reactions. That accessory factors other than the presence of depressor substance exist we unhesitatingly agree. Foremost among these is distension, and especially, in our opinion, rhythmic alteration in the degree of distension, as occurs in the course of peristalsis. Whether the significance of distension lies in a nervous mechanism, its influence on absorption, or the further production of depressor substance, is as yet not completely established. Our present bias is towards the last two factors. To a lesser degree loss of fluid may contribute to the circulatory collapse, but in no case, even in very long loops, can dehydration alone be sufficient to account for death.

The origin of depressor substance from the tissues of the gut wall as the result of changes within them, shortly after the onset of strangulation, has been demonstrated, and accords with physiological possibilities. This origin serves to differentiate it from any form of toxæmia previously described. Toxæmia has been attributed by most workers to changes occurring inside the gut lumen. Whipple, it is true, held strongly that the toxin of simple obstruction originated from the mucosa after twenty-four hours, but the fact that the depressor substance investigated by us is readily dialysable serves as a point of differentiation from his toxic proteose. Holt believed that a toxin arose in the later stages of strangulation from bacterial action on the gut wall.

While we do not dispute that bacterial invasion of devitalized tissue and subsequent proteolytic action may produce further toxic substances from the tissues of the gut wall in the latter stages of strangulation where the viability of the gut is

impaired, the early origin demonstrated for depressor substance, when the gut lumen was washed through and contained only saline, in our view definitely precludes a bacterial origin.   In the light of this factor it is necessary to review the results of previous experimental study in relation to the early collapse of intestinal strangulation.   Although the peritoneal absorption of toxic substances was recognized by Foster and Hausler in the late stages of short-loop strangulation, the initial collapse in severe cases of the long-loop type was ascribed to 'shock', although no precise evidence as to its causation was advanced.   Holt, in repeating these experiments, again differentiates between the cause of death in short and long loops, in the latter case believing that death was entirely due to loss of fluid from the circulation.   By cross-circulation experiments this latter view has been shown to be untenable.   As will be seen from his method of forming loops by individual venous ligature with patent lymphatics, it is precisely in this type of case that lymphatic absorption of toxic substances most readily occurs.   We therefore hold on the basis of present evidence that the early collapse of severe cases of intestinal strangulation may be attributed to toxæmia from the absorption of depressor substance. Distension is undoubtedly an important contributory factor.   Loss of fluid plays a variable and entirely accessory rôle, becoming more important the greater the length of the gut affected.   Hypochloræmia and bacterial toxæmia are without significance at this stage.   In the later stages, if the gut viability is impaired, this toxæmia may be reinforced by a further process.   Bacterial invasion of the devitalized tissue may, as Holt suggests, produce further toxins by proteolytic action.

A study of our results shows that there is a rough correspondence between the survival period and the length of loop involved.   We do not on this account think that it is justifiable to segregate cases of strangulation into arbitrary groups classified according to the length of gut involved, with a *different* pathogenic factor for each group.   Where longer loops are affected, fluid loss of course plays a more important part, but with such loops there is necessarily a larger area for the production of toxic substances.   In very short loops, less toxin being produced, life may be prolonged sufficiently to allow the latent period for the development of the toxæmia of the associated simple obstruction to be passed, and this may contribute to the collapse in the later stages.   In general it may be said that the significance of the length of loop would seem to lie in the increased or decreased potential area for the formation of toxic substances.   We have shown that of greater importance than the length of loop involved is the severity of the strangulation. Admittedly the combination of length with severity as in superior mesenteric strangulation gives the most rapidly fatal result, but with smaller loops of equal length, the severity is the determining factor, which accords with clinical experience.   It has been shown that the more severe strangulation is accompanied by more rapid appearance of depressor substance in the peritoneal fluid and thoracic duct, and in certain cases by greater concentration in the gut blood.

It has been shown that in those cases where, as is usual in the human, the mesenteric lymphatics are compressed, the ultimate route of absorption is by way of the peritoneal cavity, and that this only contains depressor substance when the strangulation is severe.   Our results show that dye-stuffs will be absorbed into the circulation via the lymphatics, if introduced into the tunica vaginalis or the peritoneal cavity.   There seems no justification, therefore, for the view sometimes expressed that an enterocœle in a closed hernia sac should be regarded as an extraperitoneal

structure, and, therefore, comparable to a simple obstruction. The lesser mortality shown statistically in these cases is far more probably due to early diagnosis. The significance of absorption via the thoracic duct from the peritoneum is seen from the fact that any substance delivered by this route reaches the circulation directly without the possibility of detoxication by the liver, and so may produce a progressive action despite gradual elimination by the kidney. The similarity of the urinary reactions of strangulated and injected cats and those of human patients with known strangulation suggests that the same or some closely allied depressor substance is present in the human. If this is so, certain interesting considerations arise. What rôle, if any, does renal function play in determining the fatal outcome of a case of strangulation? Does treatment by saline therapy and infusion, which, as already shown, is not directed to the cause of the collapse, produce the beneficial effect sometimes observed through its associated diuretic action? Finally, what is the significance of the release into the circulation of that portion of depressor substance which is dammed up in the veins and lymphatics of the strangulated loop? In a patient who is in good condition the release of this substance into the circulation must be well tolerated; but in the toxic case the sudden release into the circulation of a large dose of depressor substance, which, as already shown, causes a profound and permanent lowering of the blood-pressure, may be sufficient to determine a fatal outcome. Should we, therefore, in these cases make an attempt to remove the toxic substance in the peritoneal fluid and gut wall, and, having regard more to the viability of the patient than to the viability of the gut, should excision of the affected segment be performed?

Admittedly the smallest operation consistent with the pathological condition of the gut is held to give the smallest mortality. But many observers believe that once distension and toxæmia have set in, only resection can save the patient. The statistical figures give no information which truly illustrates this point, but it would be interesting to compare the results of resection and relief *in comparable cases of equal severity*. Alternatively, there remains the hope that further research may reveal some method of combating the effects of the toxin. These, together with the other points mentioned in the text, are subjects of continued investigation.

SUMMARY

1. The importance of the factor of venous strangulation as opposed to simple obstruction is emphasized.

2. Dehydration and hypochloræmia are shown to be inadequate to account for the fatal outcome of strangulation even in very long loops.

3. The production of a toxic substance from changes in the tissues of the gut wall within one hour of the onset of strangulation is demonstrated.

4. This substance produces a characteristic and persistent depression of blood-pressure which corresponds to the clinical picture of strangulation.

5. Where the mesenteric veins and lymphatics are compressed, this substance is ultimately absorbed through the peritoneal fluid and thoracic duct.

6. The relief of experimentally produced strangulation results in deterioration of the animal's condition, presumably owing to the flooding of the circulation with the accumulated toxin which is shown to appear in the mesenteric lymphatics and veins after a period of strangulation.

7. This toxic substance has been recognized both in the urine of experimental animals and human patients with known strangulation.

In conclusion we would like to take this opportunity of expressing our thanks to Mr. S. P. Steward and the members of the Technical Staff of the Royal College of Surgeons Research Department and of the Buckston Browne Farm for their expert assistance at all stages of this investigation.

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SHORT NOTES OF RARE OR OBSCURE CASES

A CASE OF HAIR-BALL OF THE STOMACH AND DUODENUM IN A CHILD OF 3½ YEARS

By G. GORDON BRUCE

SURGEON, ROYAL ABERDEEN HOSPITAL FOR SICK CHILDREN
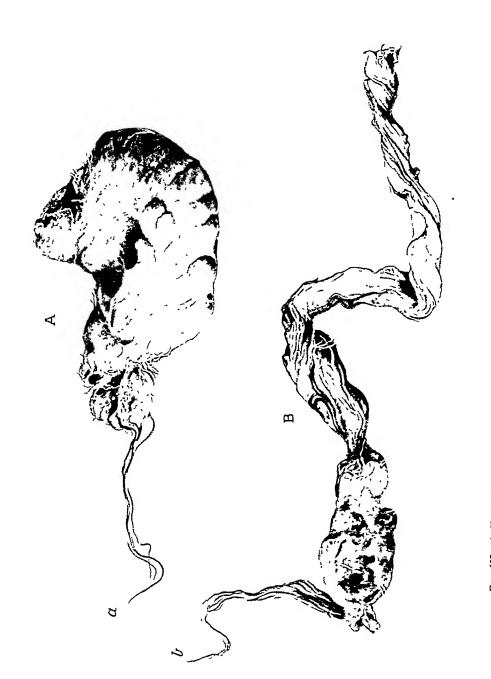
A BOY, aged 3½ years, was admitted to the Royal Aberdeen Hospital for Sick Children under my care on June 7, 1934.

HISTORY.—His mother stated that he had been a healthy child till November, 1933, when he had an attack of sickness and vomiting which lasted a week but subsided after a dose of castor oil; from then onwards he appeared fretty and

FIG. 624.—Radiograph showing filling defect in stomach—
and third part of duodenum

often woke up crying. Five months later he was seized with acute abdominal pain and diarrhœa, and received treatment in hospital for anæmia and an enlarged spleen. His condition improved, only to relapse again in June, when he was treated in another hospital without success. He had never been jaundiced. His family history was negative.

Fig. 625.—A, Hair-ball removed at operation; B, Hair-ball passed per rectum three days after operation.

ON EXAMINATION.—The child looked thin and dehydrated, fretty, and restless. His temperature was 98°, pulse 128, respirations 28. His tongue was furred and his breath foul. The abdomen was distended. In the epigastric angle and beneath the left costal margin a large solid mass could be felt which moved with respiration and was not tender. In shape it suggested a cast of the entire stomach and appeared obviously gastric in origin. The liver, spleen, and kidneys were not palpable. The stools were pale and clay-coloured. Bile was present in the urine, which was otherwise normal. The vomit consisted of altered food and bile.

Upon radiographic examination, shadows suggestive of beads were seen in the region of the fundus of the stomach, and it appeared unlikely that such would remain in a child's stomach unless entangled in a foreign substance. A hair-ball of the stomach was suspected. On questioning the mother, it was found that she had seen her boy picking wool off his jersey and eating it; he also plucked wool out of the mats and pulled out his own hair. A barium meal showed a large filling defect in the stomach (*Fig.* 624).

An attempt was made to improve the boy's health with small feeds, salines, etc., but his condition rapidly deteriorated; the vomiting became more persistent and the child more and more dehydrated. Although he appeared a serious risk, I decided to delay operation no longer.

OPERATION (June 17).—Gas and oxygen anæsthesia. The abdomen was opened through a right paramedian incision and the stomach was found almost completely filled with a soft, semi-solid substance which extended from the cardiac end through the pylorus. The surrounding viscera were packed off with moist gauze strips and the stomach was opened by an incision at right angles to the greater curvature. A large, greenish mass (*Fig.* 625A) approximately 6 in. × 3½ in. composed of hair, wool, and string was delivered with difficulty from the stomach. It could not be completely withdrawn on account of a few strands of string which extended through the pylorus into the duodenum. These were divided, the hair-ball extracted, and the incision in the stomach wall was closed with two layers of sutures.

SUBSEQUENT HISTORY.—Three days after operation the child passed per rectum a long mass (*Fig.* 625B) 14 in. in length and about 3½ in. in circumference composed of the same substances as the hair-ball removed from the stomach. From its length, the second hair-ball must have extended through the duodenum to beyond the duodeno-jejunal junction, and had prevented the extraction of the gastric mass until the communicating strands were divided as they passed through the pylorus.

Convalescence was stormy. A few days after operation crepitations could be heard at both bases, and four days later dehiscence took place. Several feet of bowel prolapsed through the wound, and a ragged tear was found in the jejunum from which intestinal contents exuded. The patient was transferred to the operation theatre without delay, when the jejunal opening was repaired, the intestine returned to the abdomen, and the abdominal wall closed with through-and-through sutures of silkworm gut. He recovered and is now in excellent health. A barium meal shows the stomach to be normal.

HÆMANGIOMA OF THE EPIDIDYMIS

BY A. L. D'ABREU

SENIOR ASSISTANT IN THE SURGICAL UNIT, THE WELSH NATIONAL SCHOOL OF MEDICINE,
THE ROYAL INFIRMARY, CARDIFF

CYSTIC and inflammatory swellings of the epididymis are common. Solid tumours are extremely rare, and fall into three groups (Rubaschow[1]): (1) Heterotopic tumours arising from embryonal rests; (2) Carcinoma arising from specific epididymal tissue; (3) Tumours arising from local neutral tissues such as sarcoma, fibroma, and lipoma. The case of hæmangioma recorded here must be placed in the third group.

E. P., aged 28, was admitted to the Surgical Unit of the Welsh National School of Medicine on Aug. 31, 1935, complaining of a swelling in the right side of the scrotum of six weeks' duration. On awakening one morning he felt a little pain and was astonished to find a swelling there. He was emphatic that there had been no trauma. At the end of ten days the pain had disappeared and the swelling had decreased in size. There had been no urethral discharge nor any difficulty in micturition.

FIG 626 —Appearances seen after the testis had been bisected The epididymis is replaced by spongy hæmangiomatous tissue The body of the testis is compressed and there is blood-clot in the tunica vaginalis The arrow indicates the line of division between the angioma above and the compressed testicular tissue below.

ON EXAMINATION.—When he presented himself for examination six weeks later, a well-developed and healthy man, the right testicle was twice the size of the left, which was normal in all respects. The epididymis appeared to be fused with the body of the testis for no separation of the two structures could be appreciated by digital examination. The skin of the scrotum in front of the testis was slightly adherent to an underlying mass, which was firm in consistency and felt moderately heavy to the supporting hand. Testicular sensation was absent. The constituents of the cord were normal on palpation. These findings betokened a syphilitic origin, but the Wassermann reaction was negative.

A diagnosis of malignant disease of the testicle was therefore made because of the painless enlargement, the skin adherence, and the absence of signs of infective epididymo-orchitis. To exclude the possibility of a tumour containing chorion-epitheliomatous tissue, fresh morning urine was sent to the Pregnancy Diagnosis Station of the Pathological Department of the Welsh National School of Medicine, where Dr. J. Gough carried out the Friedman test. He reported that the reactions in the rabbits tested were negative and that chorionepithelioma could be safely excluded from the diagnosis.

OPERATION.—The cord having been mobilized and divided at the internal abdominal ring, the testicle with the adherent skin and the entire tunica vaginalis was removed in one piece. Convalescence was uneventful and the wound healed by first intention.

PATHOLOGY OF THE REMOVED TISSUE (*Fig.* 626).—The tunica vaginalis contained recent blood-clot in the process of organization: the skin adherence noted before the operation was due to this process, the subcutaneous tissues and the blood-clot in the tunica vaginalis having undergone fibrotic organization. The origin of this blood was soon obvious, for the whole of the epididymis appeared to be replaced by thin-walled angiomatous tissue which had given way in several places with extravasation of blood. Microscopically (*Figs.* 627, 628) this tissue was characteristically that of a cavernous angioma, and only a few epididymal tubules

FIGS. 627, 628.—The microscopical appearances of the tumour.

were seen. The body of the testis was compressed from above by the angiomatous mass. No evidence either macroscopically or microscopically of a malignant neoplasm could be found.

I can find details of only one other case, that recorded by J. P. Hosford.[2] His patient was a youth of 15 who complained of a rapid enlargement of the right testis following a blow. On examination the organ was enlarged to twice its normal size, firm in consistency, and not tender; the epididymis could not be felt. Five years after orchidectomy the patient was alive and well. An examination of the specimen revealed the normal body of the testis compressed from above by a mass a little larger than itself consisting of a cavernous angioma which replaced the epididymis; no elements could be found to suggest a teratomatous origin.

I am indebted to Dr. J. Gough for his kindness in carrying out the Friedman test.

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A CASE OF MESENTERIC TUMOUR

BY A. WALLIS KENDALL

ASSISTANT SURGEON TO KING'S COLLEGE HOSPITAL

E. F. P., male, aged 49, a shop-assistant, was admitted to hospital under my care on Sept. 9, 1935.

HISTORY.—For the past nine years the patient had complained of indigestion, which had become worse during the last six months. After meals he experienced a sense of fullness and also a dull aching sensation in the left iliac region. There was no vomiting. He stated that he was becoming constipated but that he was able to correct this by taking liquid paraffin. He had noticed no disturbance of micturition during the day, but latterly had been obliged to get out of bed once each night. He was unaware of having an abdominal swelling previous to having been examined. He stressed the fact that none of his symptoms was in any way severe.

ON EXAMINATION.—A mass could be seen to cause some prominence of the lower central abdomen, extending from the symphysis pubis to the level of the umbilicus. The swelling was roughly oval in shape, but there was a prominent boss, the size of a tennis-ball, projecting from the upper right pole. The upper and lateral borders were rounded and well-defined. The lower border could not be made out, but it was obvious from the fact that it was beyond the reach of the examining finger in the rectum that the swelling could only extend a short distance below the level of the symphysis pubis. Apart from an indefinite suggestion of division into large lobules the surface was smooth. The consistency was firm and fluctuation not obtained. The swelling could be moved easily from side to side over a short distance. Palpation was quite painless. There were no signs of free fluid and no other abnormality discoverable in the abdomen. An intravenous pyelogram showed a normal urinary tract. A blood-count showed 5,500,000 red blood-corpuscles and 20,000 white blood-corpuscles per c.mm.; hæmoglobin 92 per cent; colour index 0·83.

OPERATION.—On Sept. 17 the peritoneal cavity was opened through a mid-line lower abdominal incision. There was no free fluid present in the peritoneal cavity. The tumour was found to be attached above to the mesentery of the small intestine in close proximity to the gut, and below deeply in the pelvis to the posterior aspect of the bladder on the left side. In each case a pedicle was present, the upper being shorter, wider, and considerably more vascular than the lower. The bulk of the tumour was delivered through the abdominal incision with the attached loop of small intestine. The pedicle ($\frac{1}{2}$ in. long $\times$ $1\frac{1}{2}$ in. wide) to the mesentery, whose vessels were several times their normal size in this situation, was ligatured and cut across and the small intestine set free from the tumour. The blood-supply to the intestine did not appear to be interfered with. The lower pedicle ($1\frac{1}{2}$ in. long $\times$ $\frac{3}{4}$ in. wide), which had only one or two small vessels in it, was now also ligatured and cut across. The tumour having been removed, the patient was placed in the Trendelenburg position and the intestines were packed off. It was then seen that in addition to the stump of the lower pedicle there was also a small raw area in a corresponding position on the right posterior aspect of

the bladder where adhesion to the tumour had occurred. Both the pedicle stump and this area were buried and the abdomen closed.

The patient made an uneventful recovery and was discharged from hospital on the fourteenth day.
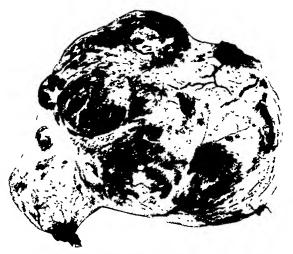
FIG 629.—Photograph of tumour after removal. ($\times \frac{2}{5}$.)
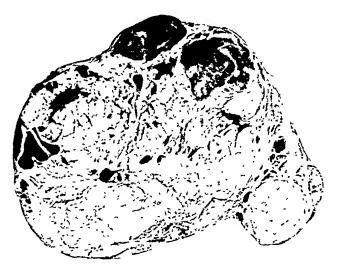
FIG. 630.—Photograph of tumour after section. ($\times \frac{2}{5}$.)

It will be seen from the photographs (*Figs.* 629, 630) that the tumour, which weighed 2 lb. $9\frac{1}{2}$ oz., is partly cystic but is for the greater part solid. There is some attempt at fibrous encapsulation of portions of the mass, particularly noticeable in the projecting upper pole. Except at the points of attachment the tumour is covered by peritoneum, underneath which can be seen large thin-walled veins.

On section the cystic, hæmorrhagic, and yellowish degenerative areas gave an appearance not unlike that of an advanced hypernephroma (*Fig.* 630).

Histological examination (*Fig.* 631) of different parts of the tumour was made by Dr. Creed, to whom I am indebted for the following report: "The section shows a sarcomatous growth which varies in appearance in different parts of the tumour. In the solid parts the growth is spindle-celled and the cells are arranged in whorls. In the more cystic part there is more production of collagen and the tumour is more fibrosarcomatous, with trabeculæ of dense fibrous tissue. The tumour is very vascular, but the vessels are well-formed, and show a good deal of hyaline degeneration."
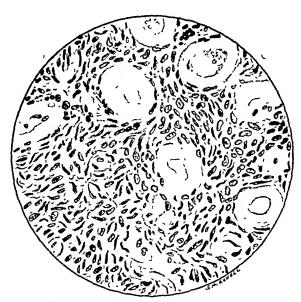
FIG. 631.—Histological appearance of tumour. (× 200.)

Comment.—Though of rare occurrence, a sufficient number of mesenteric tumours have been described in the literature to show that considerable variation in their pathological nature exists. About half are malignant in type, and of these only one-third are removable at operation. Particular reference must be made to the article by Phillips,[1] who publishes a series of 2 solid mesenteric and 4 retroperitoneal tumours, and suggests, on strong pathological grounds, that these two groups be classed together as paramesenteric tumours. In practically every recorded case the slightness of the symptoms in the presence of a large tumour is noted. In spite of the pathological nature and size of the growth described here it is interesting to note the absence of technical difficulties in the way of its removal, and also the apparent freedom from metastasis.

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A LARGE LEIOMYOMA OF THE PROSTATE

By T. W. MIMPRISS

CHIEF ASSISTANT, SURGICAL UNIT, ST. THOMAS'S HOSPITAL

A LABOURER, aged 60, was admitted to hospital with acute retention of urine. During the previous year he had suffered from progressive frequency of micturition; in the month before admission he had had a daily frequency of nine and nocturnal frequency of five or six times. The stream was poor and he experienced difficulty in beginning the act. There was a history of one recent attack of acute retention, relieved by catheterization. No other urinary symptoms had been noted.
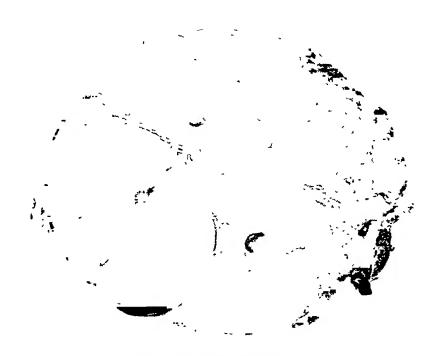
FIG. 632.—Leiomyoma of prostate. ($\times \frac{2}{3}$.)

ON EXAMINATION.—The patient was a healthy man whose bladder extended to the umbilicus. Rectal examination showed a very large prostate, only the lower part of which could be examined by the finger. The gland was smooth and firm, suggesting the common type of prostatic enlargement. Gradual decompression by means of an indwelling catheter was carried out over a period of twenty-four hours. No abnormality was detected in the respiratory and cardiovascular system, the blood-pressure was 150/90, the blood-urea 32 mgrm. per 100 c.c., and the urine free from infection. Indwelling catheter drainage with twelve-hourly bladder washes was carried out for ten days. In view of his good condition a one-stage suprapubic prostatectomy was then performed.

OPERATION.—Under ether anæsthesia the prostate could be palpated through the abdominal wall. On opening the bladder an enormous prostate was found. It surrounded the urethra and appeared to be an extreme example of the ordinary type of prostatic enlargement. Owing to its size it was impacted between the body of the pubis in ·front and the sacrum behind. The tumour could be enucleated from its capsule with ease, but great difficulty was experienced in reaching the lower part of the tumour, as it filled the pelvis almost completely. Enucleation therefore involved considerable manipulation and some degree of hæmorrhage.
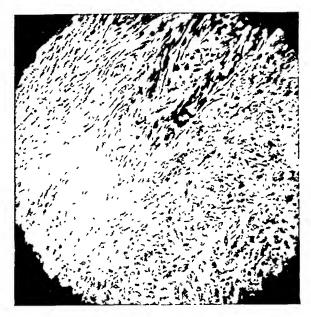
FIG. 633.—Low-power view of section of tumour.

The patient was much shocked at the end of the operation and died twenty hours later.

PATHOLOGY.—The specimen (*Fig.* 632) weighed 19 oz. and measured 5·6 × 4·4 × 2 in. Macroscopically it was of the same structure throughout. Numerous sections (*Figs.* 633, 634) of the gland submitted to microscopy showed the structure of a leiomyoma ; no section showed any trace of glandular tissue.

Discussion.—It is recognized that small leiomyomatous nodules are found comparatively frequently in enlarged prostates. Large leiomyomata are rare.

Dial and Halpert[1] in 1933 reviewed the literature on this subject and divided the cases into two groups, depending on whether the tumour caused disturbances of micturition or of defæcation. The case recorded here comes into the former group.

Patch and Rhea[2] have recently reported a case of this type, together with a review of the literature. Including their own case, they find only 11 cases of large leiomyomata reported. They also point out that in some of the recorded cases

the tumour was attached to the prostate by a pedicle, as occurred in Hinman and Sullivan's[3] first case, or was situated in a position remote from the urethra.

In the case recorded here the tumour was peri-urethral and projected into the bladder. Before the specimen was enucleated it resembled exactly the usual type of prostatic enlargement. The weight of the specimen (19 oz.) is remarkable. A search of the reports of large prostatic tumours of any type suggests that it is the second largest recorded. Neupert[4] reports a retroperitoneal tumour weighing $7\frac{1}{2}$ lb., which was considered to be a large leiomyoma in connection with the prostate. The case report, however, is not very explicit. Apart from this, the
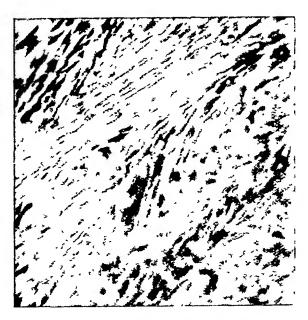
FIG. 634 —High-power view of section of tumour.

largest recorded tumours I can find are those of Fullerton[5] (17 oz.) and Freyer[6] ($16\frac{3}{4}$ oz.). Both of these tumours were of the ordinary type of prostatic enlargement.

I wish to thank Professor L. S. Dudgeon for his advice and pathological report on the specimen, and Mr. W. H. C. Romanis for permission to publish the case.

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A LIPOMA OF THE COLON

By KEITH ROSS

HONORARY SURGEON, GEELONG HOSPITAL, AUSTRALIA

LIPOMATA of the colon are so rare that the clinical notes of a new case may be of sufficient interest to warrant their publication.

Mrs. M., aged 40, had suffered for some months from flatulence and discomfort in the epigastrium. The discomfort usually occurred soon after meals and was relieved to some extent by regulation of the diet on ' ulcer ' lines. Relief, however, was incomplete, and further examination disclosed a mobile rounded tumour which could be felt in the left epigastrium, only when the patient was lying on the right side. There was no disturbance of the bowels. Examination by a radiologist after a barium meal and enema showed no lesion of the gastro-intestinal tract.

Laparotomy revealed the ascending colon to be very considerably enlarged and a tumour was felt within the lumen of the colon at its hepatic flexure. The

FIG. 635.—Lipoma ulcerating through mucous membrane of colon.

tumour could be ' milked ' along to the left half of the transverse colon in one direction, and to the cæcum in the other, without causing any invagination or dimpling of the wall of the bowel. The tumour was then fixed in the cæcum and the latter delivered through a gridiron incision in the right iliac fossa. On opening the cæcum, the tumour was found to be a large oval lipoma ($3\frac{1}{2} \times 2$ in.) arising in the submucous tissue, pushing the mucous membrane before it, and ulcerating through the mucous membrane. The mobility of the tumour was due to its having a long pedicle of loose mucous membrane, and its removal was easily accomplished by cutting through the mucosa at its reflection on to the mass. The mucosa was sutured, and as soon as it was let go it sprang sharply back up the ascending colon. The cæcum and abdominal wounds were closed and the patient had an uneventful convalescence.

The tumour, which is shown in *Fig.* 635, has been carefully examined and found to consist of fatty tissue only.

LOCAL PLASTIC PERITONITIS, POSSIBLY DUE TO INCARCERATION OF INTESTINE IN A HERNIA, CAUSING INTESTINAL OBSTRUCTION

By KEITH ROSS

HONORARY SURGEON, GEELONG HOSPITAL, AUSTRALIA

CHRONIC adhesive peritonitis may occur as a local or a generalized condition and in varying grades of severity. In many cases it would appear that the inflammatory process originates in the female pelvic organs and spreads thence to the bowel. In others, such as the one reported here, the etiology is more obscure.

J. W., a male aged 58, was admitted to hospital with a three days' history of severe pain in the abdomen, vomiting, and absolute constipation. Previously, apart from a mild and non-progressive constipation, he had always been healthy.

FIG 636 —Mass excised, now collapsed, but tensely swollen at operation (✗ ⅓)

He had never had an operation or suffered from any disease such as typhoid fever or dysentery. For many years he had had a right inguinal hernia and this had come down since the onset of vomiting. It was easily reduced and found to have a widely patent neck.

OPERATION.—Immediate laparotomy disclosed a large tumour consisting of a mass of ballooned and inextricably fused coils of ileum lying quite discretely below the right lobe of the liver. A grossly hypertrophied loop of ileum ran to the mass and a correspondingly small one from it. There were no adhesions to

surrounding structures, and a rapid survey revealed no other morbid process within the abdomen.   The mass was excised and the ileum re-united by a side-to-side anastomosis.   Convalescence was uneventful.

After operation the blood was found to give a negative reaction to the Wassermann test ; X-ray examination of the chest disclosed no evidence of pulmonary tuberculosis or any thickening of the pleura ; there was no evidence of renal disease.

PATHOLOGICAL FINDINGS.—The mass excised is shown in *Fig.* 636 and consists of numerous loops of ileum firmly bound together by fibrous adhesions.   At the junction of the afferent loop of ileum and the mass there is a dense white scar (not very well displayed in the illustration) and the appearance of constriction.   Water pumped into the mass from either end passes only very slowly through it.   On dissection the gut is found to loop acutely back on itself in maze-like fashion, with

FIG. 637.—Microscopic view of two fused loops.

constriction of the lumen in very many places, but there is no pathological process evident other than fibrosis.   Microscopic examination of the affected loops discloses thickening of the tunica serosa (*Fig.* 637).

Comment.—The etiology of the pathological condition in this case is obscure.   So far as can be ascertained there had never been any lesion or disease of any nature whatsoever of any of the abdominal organs, nor was there any evidence of syphilis or tuberculosis.   There was, however, a wide-necked hernia and this had frequently contained bowel.   Bowel which has remained for any length of time in a hernial sac not infrequently shows evidence of chronic peritonitis, and it appears reasonable to suggest that in this case the condition had originated in one or more loops of ileum that had been retained for some time in the hernial sac ; later when the gut returned to the abdominal cavity the pathological process continued and extended.   This explanation is purely hypothetical, but on the evidence available it appears to be the most reasonable.

TRANSFIXION OF THE AORTA

BY KENNETH EDMUNDSON

SURGEON IN CHARGE, THE HOSPITAL, TUKUYU, TANGANYIKA TERRITORY

THE following case would appear worthy of record because the patient was still alive thirteen hours after he had received an apparently fatal wound, and because the inflicting weapon acted as a preventive to further damage. The facts are as follows :—

A male African was brought into hospital at 1 p.m. by motor-car from a distance of fifteen miles. He had been wounded by an arrow, being shot at close quarters the evening before at 11 p.m. He was in no obvious distress on arrival at hospital and walked unaided from the car to the operating-theatre, a distance of some fifty yards.

ON EXAMINATION.—The iron shaft of an arrow-head protruded 1 in. from the sternum. It was about $\frac{1}{2}$ in. to the right of the mid-line and opposite the second interspace. It protruded almost at right angles to the sternum, the direction being backwards and slightly upwards. This shaft was seen to vibrate rhythmically with the pulse, and on placing the finger lightly on the tip a transmitted thrill was felt. On auscultation near the shaft a loud musical murmur was audible, which was conducted up into the neck on the right side. The pulse on admission was 100. There had been very little external hæmorrhage up to this time, although obvious endeavours had been made to cut and pull the arrow-head out.

Soon after admission the wound began to bleed and the pulse quickened to 120. Morphia, $\frac{1}{4}$ gr., was given and firm pressure with swabs was applied over the wound. The hæmorrhage subsided. It was then decided to try to remove the arrow-head, as it was judged to be held under the innominate.

OPERATION.—Under slow chloroform and ether anæsthesia an incision was made in the mid-line of the sternum and the skin reflected. An oblong window, 2 in. by 1 in., was made in the sternum. The bone was lifted up over the arrow-shaft. The anterior mediastinum contained blood-clot, but no fresh bleeding was encountered on the removal of the window of bone. The lower barb of the arrow was first freed from tissue and then the upper, and the arrow was withdrawn. Its withdrawal was immediately followed by a very severe hæmorrhage. The patient died almost immediately.

POST-MORTEM EXAMINATION.—This was made as soon as possible after death, and showed the following facts. There was complete transfixion of the aorta by the arrow, which had entered the ascending portion on its convexity and had penetrated the posterior wall at the junction of the innominate and the aorta. The inner coat of the vessel showed superficial excoriations as if the point of the arrow had been moved to and fro in the lumen. There was no marked internal hæmorrhage, nor injury to the pleura or pericardium. The hæmatoma in the track of the arrow was inconsiderable and the hæmorrhage had not extended down into the posterior mediastinum.

Conclusion.—The arrow had pierced the sternum in such a manner that the two barbs just impinged on the under surface of the sternum, the point being fixed by the barbs in the aorta and the tissues posterior to it. There was thus formed

an immovable splint, which completely filled the incisions made and which the musculature of the vessel gripped and rendered efficacious. Removal of the plug formed by the arrow-head was followed by splitting of the muscle under the pressure and instant death.

The extraordinary feature of the case is the fact that the man had lived for over thirteen hours, and, in spite of the efforts of his friends to remove the arrow by cutting and pulling, survived until its removal by modern methods.

REVIEWS AND NOTICES OF BOOKS

Post-graduate Surgery. Edited by RODNEY MAINGOT, F.R.C.S., Senior Surgeon to the Royal Waterloo Hospital, etc. With an Introduction by the Right Hon. LORD MOYNIHAN OF LEEDS, K.C.M.G., C.B., M.S., F.R.C.S. In three volumes. Royal 8vo. Vol. I: Pp. 1742 + xvi, with 846 illustrations. 1936. London: Medical Publications Ltd. £9 9s. the set, or £3 10s. per volume.

THIS great work on surgery has a very definite aim and scope. It presents the subject in a practical way, so that qualified surgeons may have a guide in their work and a book of reference in their reading. Basic knowledge of surgery is assumed, and the space is devoted to the description of special methods of investigation, special methods of treatment, including operative technique, and the management of cases both before and after operation.

The team of writers who have collaborated in producing this work is notable in two respects. In the first place it includes many young men—a fact which gives the best guarantee that the book shall be really up-to-date. And secondly it includes a large proportion of physicians (actually seven out of twenty in this first volume), which indicates that the treatise is no mere technical description of operative procedure, but a reasoned study of patients and of pathological processes. The present volume opens with an introduction by Lord Moynihan, who speaks of the needs of the post-graduate student and the high ideals of surgery.

Part I deals with anæsthesia (Langton Hewer). There is a clear account of anæsthetic methods, preference being given to gas–oxygen for inhalation and percaine for spinal anæsthesia. A cautious and critical account of premedication methods and of evipan is given.

Part II deals with the abdomen. This section occupies the greater part of the volume (nearly 1200 pages), but only includes the surgery of the alimentary tract, glands, and spleen. Preliminary chapters on the investigation of a case of dyspepsia are by Maingot, Sleigh Johnson, and Deville. The common diseases and the usual operative procedures on the stomach and duodenum are clearly described and well illustrated by Maingot, and then follows a special chapter on the Billroth I operation of gastrectomy by Finochietto (Buenos Aires) with a great number of detailed illustrations. Hurst writes on the medical treatment of gastric, duodenal, and anastomotic ulcer. In his opinion, if suitable treatment is given for a sufficient period, nearly every gastric ulcer eventually heals, as well as about 75 per cent of duodenal ulcers, and 50 per cent of the much more intractable anastomotic ulcers which follow gastric operations.

The chapters on the gall-bladder and bile-ducts are by Maingot, Moore, and Dickson Wright. In addition to good illustrations of diseased conditions and operative procedures there is a series of excellent diagrams of the mistakes and accidents which may occur in the performance of cholecystectomy.

The chapters on the liver are by Dickson Wright and Sleigh Johnson. Rupture of the liver is dismissed in half a page, but great space is devoted to liver function and jaundice. The diseases and injuries of the spleen are very fully discussed by Maingot, whilst the rôle of radiotherapy in splenic diseases is described by Levitt, and Egyptian splenomegaly by Stiven.

Appendicitis and its complications and treatment are described by Hamilton Bailey in a most lucid and helpful chapter. A very fair via media between the extreme views about treatment of the more-than-48-hours case is provided. This takes the form of laying down the rule of expectant treatment except under five circumstances. The whole article is very helpful in its clear advice and directions for treatment. In cases where pylephlebitis is feared, it is suggested that the ileocolic vein should be ligated before removing the appendix. We think that tuberculous peritonitis should be referred to in the differential diagnosis.

Wakeley, in his beautifully illustrated article on the surgery of the colon, gives a very complete and practical summary of diagnosis and treatment. He regards the two-stage methods and that of Devine with favour.

Over 200 pages are occupied by articles on intestinal obstruction and peritonitis by Cokkinis. In addition to the more or less routine description of varieties and types of obstruction there is an excellent discussion of the underlying pathology and physiology of the condition. The summary of treatment of a case of paralytic ileus given in fourteen sentences will appeal to every surgeon who wants simple and clear guidance in dealing with this desperate condition. We think it a pity that one or two coloured illustrations are not given in this section in place of many of the black-and-white figures, which fail to show the condition of congestion or gangrene. A posthumous article by Tyrrell-Gray on paralytic ileus is full of interest, but we are rather surprised that this subject should have been treated twice by different authors. The complications following abdominal operation are dealt with in a very practical way by Maingot.

Part III is occupied entirely by the section on diseases of the anus and rectum by Miles (220 pages), and is wonderfully complete and informative. The description of common ailments, piles, and fistulæ is very complex. The incidence of piles appears to be governed by mathematical laws, and of fistulæ there are seventeen different varieties. The chapters on cancer of the rectum contain convincing arguments in favour of the abdomino-perineal excision. The mortality-rate has been reduced to 10 per cent by the use of spinal percaine with gas and oxygen for anæsthesia, by eliminating patients with reduced cardiac energy, and by the routine use of blood transfusion. Methods by which the anal sphincter can be retained are not mentioned, the use of radium for inoperable cases is not discussed, neither are the operative methods of dealing with intractable pain.

Parts IV and V cover the radiography of the alimentary and urinary tracts (Cecil Bull) with clear radiograms and diagrams of typical conditions; the technique of radium treatment is by Stanford Cade and Malcolm Donaldson. All these articles are very complete and well illustrated.

It remains to give an appreciation of the book as a whole. We can only say that it is very good, and we look forward to the succeeding two volumes with great interest. The days are gone when one man like Erichsen could write a complete text-book of surgery single-handed. The present volume shows wonderful team-work, with the inevitable overlapping and redundancy and conflict of views reduced to a minimum. The due weight given both to the physiological and medical aspects of surgical diseases is quite in accordance with advanced modern teaching. The paper, printing, and illustrations are all good, though we think that a few coloured figures would have been helpful.

We heartily congratulate the Editor and his collaborators on their energy and industry in producing this monumental work, which will soon be regarded as the standard English book of reference.

The Early Diagnosis of the Acute Abdomen. By ZACHARY COPE, B.A., M.D., M.S. (Lond.), F.R.C.S., Surgeon to St. Mary's Hospital, Paddington, etc. Seventh edition. Medium 8vo. Pp. 254 + xiv, with 33 illustrations. 1935. London: Humphrey Milford, Oxford University Press. 10s. 6d. net.

THOUGH we much dislike the term 'acute abdomen', and would vastly prefer the title to have been "The Early Diagnosis of Acute Abdominal Crises", yet we gladly acknowledge this little book to be of the greatest service and undoubtedly the best of its kind. It has now reached its seventh edition—a fact which speaks, literally, 'volumes' for its efficiency. The most important addition is a description, with two figures, of the use of X-rays in the diagnosis of acute intestinal obstruction, a method which is extensively employed in America though only to a small degree as yet in this country. Where, as in hospitals, the requisite apparatus is available, most valuable information can be thus obtained, especially with regard to the extremely important question whether the site of obstruction is in the small or the large intestine. We are glad to note that the author does not describe intussusception under acute intestinal obstruction but allots it a chapter to itself. It is important to recognize that acute intussusception is not primarily an obstruction but rather a 'displacement' or 'dislocation' of the bowel, and that the object of early diagnosis and treatment of this condition is to prevent it from ever becoming an obstruction. We disagree profoundly with the statement on p. 117 that "it is a mistake to treat strangulated external hernia in a different category from obstruction in which no external cause is to be found". It is only by gross carelessness that strangulated hernia can be overlooked even in its earliest stages, so that its mortality should be, and

is actually, much less than that of other cases of obstruction, where, there being no external swelling, the diagnosis and treatment are alike much more difficult. To include strangulated hernia with these latter is to reduce very materially the total mortality, and the same criticism applies to the inclusion of intussusception. Thus, in the largest series of cases of acute intestinal obstruction yet published—that of 6892 cases collected and presented to the Section of Surgery at the Centenary meeting of the British Medical Association in 1932 by Vick— the mortality of all forms together was 26·2 per cent. If strangulated hernia is excluded (whose mortality was 17·8 per cent), the mortality is increased to 38·8 per cent, and if, further, idiopathic intussusception is excluded, the mortality becomes 39·9 per cent. This is the real mortality of those cases of acute intestinal obstruction the cause of which is not readily obvious, and it is this appalling mortality of nearly 40 per cent that clamours for the exercise of every means of early diagnosis : only thus can we hope for its material reduction.

The author rightly deprecates the description—strongly insisted upon elsewhere—of acute appendicitis and acute appendicular obstruction as two separate entities. To stress such distinction is rather apt to lead to the conclusion that cases of acute appendicitis without obstruction do not need immediate operation—a most pernicious doctrine. The severity and frequency of the vomiting at the onset of acute appendicitis indicate, as the author correctly states, the degree of distension of the appendix, and, consequently, the immediate risk of perforation. In Chapter V is an excellent account of the differential diagnosis of acute appendicitis, and the misleading absence of abdominal rigidity in pelvic appendicitis is properly emphasized.

We have never seen a patient " writhing in agony " at the onset of perforation of a gastric or duodenal ulcer ; on the contrary, although he may scream in his agony, his muscular efforts are directed to keeping his abdomen as still as possible. The contrast between the abdominal stillness and rigidity of a case of perforated gastric ulcer and the extreme restlessness and abdominal flaccidity of one of rupture of an ectopic pregnancy is most impressive.

Acute pancreatitis receives an excellent description, and emphasis is rightly laid upon the profound degree of shock that usually accompanies the pain, the persistence of the severe pain in the back, and the marked cyanosis of the face and extremities. The last chapter is one of the most useful in the book, and deals with those diseases which simulate acute abdominal crises. The table of differences between acute thoracic inflammations and acute abdominal crises on p. 236 will well repay most careful study.

The book is clearly written, and the simplicity of the illustrations is a fitting accompaniment to the extreme lucidity of the author's method of expression.

The Early Diagnosis of Malignant Disease. By GEOFFREY KEYNES, M.A., M.D. (Cantab.), F.R.C.S., Assistant Surgeon to St. Bartholomew's Hospital, etc. F'cap 8vo. Pp. 70. 1935. London : John Bale, Sons & Danielsson, Ltd. 2s. 6d. net.

THIS book has the merits of brevity, clearness, and low price, and will be very helpful to the general practitioner. It fails, however, to state clearly that the main duty of a practitioner who suspects early cancer is to obtain for the patient an expert opinion. Mr. Keynes thinks the use of the terms ' malignant ' and ' malignancy ' encourages pessimism. He insists on the fact that really early cancer is local, and therefore often curable, and that whatever progress is made in surgical and radiological technique, the end-results will not improve unless diagnosis becomes earlier and more precise, and patients become more ready to seek early advice. He thinks the practitioner should teach the public that early cancer is painless and often curable. He should be ready to act on suspicion only and should develop an attitude of mind which, if it occurred in the patient, would be a morbid cancer-phobia.

While not blind to its difficulties, the author thinks that an annual general overhaul would be a step towards the earlier detection of cancer. The importance of radiology is stressed, especially in suspected cancer of the stomach and bowel. The various forms of cancer are then considered seriatim from a diagnostic point of view.

In a book the general teaching of which is so sound, criticism must be confined to points of detail. It is stated that " Any breast lesion, however small, that is really hard in consistency is probably a cancer." May not a fibro-adenoma or a small cyst be really hard ? No teaching is given as to the clinical differences between carcinomatous and mastitic enlargement

of the axillary glands, and nothing is said about the importance of slight flattening of the nipple, or of the retraction of individual duct-orifices upon its surface. One must emphatically dissent from the statement that " In the great majority of breasts affected by mastitis the change is diffuse and more or less uniform." The granular thickenings of chronic mastitis when examined on the flat with two hands are generally partial and sector-shaped, affecting particular lobes or groups of lobes. They are most often felt in the upper and outer quadrant.

The section on gastric cancer is especially good, and is illustrated by X-ray tracings which show that the healing of a chronic ulcer may not prevent subsequent malignancy. The free use of radiological examination in the dyspepsia of middle life is recommended as the only means of early diagnosis. The achlorhydria seen in 65 per cent of cancers is shown to be due to previous chronic gastritis.

Mr. Keynes has fallen a victim to the prevalent fashion of regarding melanotic sarcoma as carcinoma. Surely the work of Ribbert established once for all its sarcomatous nature.

Der Schenkelhalsbruch : ein mechanisches Problem. By Dr. FRIEDRICH PAUWELS (Aachen). Royal 8vo. Pp. 157, with 186 illustrations. 1935. Stuttgart : Ferdinand Enke. Paper covers, RM. 13.60 ; bound, RM. 15.00.

A VERY excellent monograph on the mechanical factors which are involved in the production, prognosis, and treatment of fractures of the femoral neck. The subject is worked out with mathematical precision accompanied by diagrams and formulæ. Probably this somewhat abstruse presentation will repel rather than attract the average surgeon's attention ; but, on the other hand, the diagrams, X-rays, and clinical photographs are clear and convincing. We are accustomed to classify fractures of the femoral neck according to their level as between the head and the trochanter of the femur ; but this author demonstrates that it is much more important to group them according to the direction of the fracture. Thus in Grade 1 the fracture is nearly horizontal, in Grade 2 it is about 45° to the horizontal, and in Grade 3 nearly vertical. The important practical considerations are : (1) The liability to non-union is in direct proportion to the verticality of the line of fracture ; and (2) That in cases of non-union, the proper treatment is Schanz's osteotomy. In this operation a wedge is removed from below the great trochanter. Pins are inserted above and below the osteotomy, and the femur is angulated. When healing has occurred the adduction of the trochanter will have brought it below the head of the femur, the line of fracture will be horizontal, and union will take place.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest for our readers.]

Traité de Chirurgie d'Urgence (Félix Lejars). By PIERRE BROCQ, Professor agrégé à la Faculté de Médecine de Paris; Chirurgien des Hôpitaux; and ROBERT CHABRUT, Ancien Chef de Clinique à la Faculté de Médecine de Paris. Ninth edition. Large 8vo. One volume of 1286 pages, with 1250 illustrations. Paper covers, Fr. 170; bound, Fr. 190. In two volumes (Pp. 1299 + xv), Fr. 200. 1936. Paris : Masson et Cie.

A Terminology of Operations of the University of Chicago Clinics. By HILGER PERRY JENKINS, M.D. Crown 8vo. Pp. 99 + xx. 1935. U.S.A.: The University of Chicago Press; Great Britain and Ireland : Cambridge University Press. 4s. 6d. net.

Urology in Women : A Handbook of Urinary Diseases in the Female Sex. By E. CATHERINE LEWIS, M.S.(Lond.), F.R.C.S., Surgeon to the Royal Free Hospital; Surgeon and Urologist to the South London Hospital for Women. 9 × 6 in. Pp. 100 + viii, with 31 illustrations. 1936. London : Baillière, Tindall & Cox. 6s. net.

An Index of Differential Diagnosis of Main Symptoms. Edited by HERBERT FRENCH, C.V.O., C.B.E., M.A.(Oxon.), F.R.C.P.(Lond.), Consulting Physician to Guy's Hospital, etc. Super royal 8vo. Pp. 1145 + xii, with 742 illustrations (196 in colour). 1936. Bristol : John Wright & Sons Ltd. 63s. net.

Lehrbuch der Kriegschirurgie. By Dr. CARL FRANZ, Honorarprofessor der Universität, Berlin, etc. Second edition. Large 8vo. Pp. 424 + vii, with 121 illustrations. 1936. Berlin : Julius Springer. Paper covers, RM. 26.60; bound, RM. 28.80.

Zur Erkennung und Begutachtung von Schädelgrundbrüchen. By HANS HELLNER. Part 19 of *Hefte zur Unfallheilkunde.* Large 8vo. Pp. 43, with 17 illustrations. 1936. Berlin : Julius Springer. RM. 4.40.

Brompton Hospital Reports. Volume IV, 1935. Demy 8vo. Pp. 259 ÷ viii. Illustrated. London : The Secretary, The Hospital for Consumption, Brompton, S.W.3. 2s. 9d.

Das Hämorrhoidalleiden : seine Komplikationen und deren Behandlung. By Dr. KASPER BLOND and Dr. HERBERT HOFF. With a Foreword by Prof. Dr. LEOPOLD SCHÖNBAUER. Large 8vo. Pp. 121 + viii, with 50 illustrations. 1936. Leipzig and Vienna : Franz Deuticke. Paper covers, M. 12; bound, M. 14.40.

Mechanics of Normal and Pathological Locomotion in Man. By ARTHUR STEINDLER, M.D., F.A.C.S., Professor of Orthopedic Surgery, the State University of Iowa. Large 8vo. Pp. 424 + xviii, with 453 illustrations. 1936. London : Baillière, Tindall & Cox. 36s. net.

Handbook of Surgery. By ERIC C. MEKIE, M.B., Ch.B., F.R.C.S.E., Medical Officer, Malayan Medical Service. With a Foreword by JOHN FRASER, M.C., M.D., Ch.M., F.R.C.S.E., Regius Professor of Clinical Surgery, University of Edinburgh. Crown 8vo. Pp. 699 + xii, with 24 illustrations. 1936. Edinburgh : E. & S. Livingstone. 12s. 6d. net.

Zweite internationale Kropfkonferenz (Bern, Aug. 10–12, 1933). Edited by Dr. OTTO STINER. Large 8vo. Pp. 698 + li. Illustrated. 1935. Bern: Hans Huber. Sv. Fr. 25.

Tecknik und Ergebnisse der Gaumenplastik. By Dr. GEORG AXHAUSEN (Berlin), Large 8vo. Pp. 126, with 176 illustrations. 1936. Leipzig: Georg Thieme. Paper covers, M. 17; bound, M. 18.

Emergency Surgery. By HAMILTON BAILEY, F.R.C.S., Surgeon, Royal Northern Hospital, London, etc. Second edition. Demy 8vo. Pp. 842 + x, with 812 illustrations. 1936. Bristol: John Wright & Sons Ltd. 50s. net.

An Index of Treatment. Edited by ROBERT HUTCHISON, M.D., LL.D., F.R.C.P., Consulting Physician, London Hospital, and Hospital for Sick Children, Great Ormond Street. Eleventh edition. Super royal 8vo. Pp. 1020 + xv. Illustrated. 1936. Bristol: John Wright & Sons Ltd. 42s. net.

The Human Foot: its Evolution, Physiology and Functional Disorders. By DUDLEY J. MORTON, Associate Professor of Anatomy, College of Physicians and Surgeons, Columbia University. Large 8vo. Pp. 244 + xvi, with 100 illustrations. 1935. New York: Columbia University Press. London: Oxford University Press (Humphrey Milford). 15s. net.

Surgical Emergencies in Children. By HAROLD CLIFFORD EDWARDS, M.S.(Lond.), F.R.C.S., Surgeon and Lecturer in Surgery, King's College Hospital, London, etc. Demy 8vo. Pp. 274 + vii, with 99 illustrations. 1936. London: Baillière, Tindall & Cox. 12s. 6d. net.

Diagnostic Roentgenology. Edited by ROSS GOLDEN, M.D., Professor of Radiology, the College of Physicians and Surgeons, Columbia University; Director of the Department of Radiology, Presbyterian Hospital, New York. $9\frac{1}{2} \times 7\frac{1}{4}$ in. Pp. 867 + xi, with 964 illustrations. 1936. New York and Edinburgh: Thomas Nelson & Sons. $20.00.

Les petites Règles de la Chirurgie parfaite. By J. OKINCZYC, Professeur agrégé; Chirurgien des Hôpitaux de Paris. Royal 8vo. Pp. 60. 1936. Paris: Masson et Cie. Fr. 12.

The Study of Anatomy. Written for the Medical Student. By S. E. WHITNALL, M.A., M.D., B.Ch.(Oxon.), M.R.C.S., L.R.C.P., F.R.S.(Canada), Professor of Anatomy in the University of Bristol, 1935. Third edition. Crown 8vo. Pp. 113. 1936. London: Edward Arnold & Co. 4s. 6d. net.

Surgical Diseases and Injuries of the Genito-Urinary Organs. By Sir JOHN THOMSON-WALKER, D.L., M.B., C.M.Ed., F.R.C.S.Eng., Consulting Urologist and Emeritus Lecturer in Urology, King's College Hospital, etc. Second edition, revised: edited by KENNETH WALKER, M.A., M.B., B.C.(Cantab.), F.R.C.S..Eng., Jacksonian Prizeman and Hunterian Professor, R.C.S., 1911, 1922, 1924, 1933; Lecturer in Venereal Diseases, St. Bartholomew's Hospital; etc. Medium 8vo. Pp. 974 + xviii, with 283 illustrations and 25 colour and 33 black-and-white plates. 1936. Cassell & Co. Ltd. 32s. 6d. net.

A Synopsis of Surgical Anatomy. By ALEXANDER LEE McGREGOR, M.Ch. (Edin.), F.R.C.S. (Eng.), Lecturer on Surgical Anatomy, University of Witwatersrand, etc. With a Foreword by Sir HAROLD J. STILES, K.B.E., F.R.C.S.E. Third edition. Crown 8vo. Pp. 664 + xviii, with 648 illustrations. 1936. Bristol: John Wright & Sons Ltd. 17s. 6d. net.

Ueber das Zwölffingerdarmgeschwür. By Prof.-Dr. P. CLAIRMONT (Zurich). Part 7 of *Vorträge aus der praktischen Chirurgie*. Royal 8vo. Pp. 29. 1936. Stuttgart: Ferdinand Enke. RM. 1.80.

A Textbook of Surgery. By American Authors. Edited by FREDERICK CHRISTOPHER, B.S., M.D , F.A.C.S., Associate Professor of Surgery at Northwestern University Medical School, etc. Royal 8vo. Pp. 1608 – xix, with 729 illustrations. 1936. Philadelphia and London: W. B. Saunders Co. 42s.

Baillière's Synthetic Anatomy. By J. E. CHEESMAN. Part XIII. The Eye and Orbit. Plates 7½×9 in. 1936. London: Baillière, Tindall & Cox. 3s. net.

A Textbook of Roentgenology. By BEDE J. MICHAEL HARRISON, M.B., CH.M., D.M.R.E. (Cantab.), F.A C.R., Director of Department of Roentgenology, Vancouver General Hospital, etc. Medium 8vo. Pp. 826 – xxvi, with 238 illustrations. 1936. London: Baillière, Tindall & Cox. 45s.

The Life and Works of Charles Barrett Lockwood (1856–1914). By ERIC C. O. JEWSBURY, M.A., B.M., B.CH. (Oxon.). The Wix Prize Essay, St. Bartholomew's Hospital, 1934. Crown 8vo. Pp. 104 – viii, with 12 illustrations 1936. London: H. K. Lewis & Co., Ltd. Cloth, 3s. 6d. net; paper covers, 2s. 6d. net.

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